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Nomenclature report on the major histocompatibility complex, genes, and alleles of Great Ape, Old and New World monkey species

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Introduction

The major histocompatibility complex (MHC) of Great Ape, Old and New World monkey species (also referred as non-human primate (NHP) species) have attracted considerable attention from the scientific community in recent years. Certain NHP species have been studied extensively as models for human biology and disease, while other free-ranging populations have drawn attention due to issues related to species conservation or reproductive biology. The MHC, characterized by a high degree of plasticity, encodes a cluster of genes, many of which display polymorphism. Progress in nucleotide sequencing technologies has resulted in the speedy accumulation of data that complicates data-storage and annotation issues. The IPD-MHC NHP database (www.ebi.ac.uk/ipd/mhc/nhp) is an established and convenient platform to store and retrieve quality-controlled sequences of various non-human primate species. This nomenclature report represents a follow-up of the communications that were published previously (Ellis et al. 2006; Klein et al. 1990). In humans, the MHC is designated as human leucocyte antigen (HLA), and the Nomenclature

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#Curators of the IPD-MHC NHP database

Committee for the Factors of the HLA system has recently launched an adaptation to its nomenclature protocol (Marsh 2010). The way HLA-alleles are named has changed, for instance, by introducing colons. The adaptations have been implemented, wherever possible, for the non-human primate equivalents as well. Next, it is evident that different NHP species may share lineages at particular MHC loci. In the past, lineages and alleles may have been named on an arbitrary basis, depending on the moment of their discovery. The tremendous amount of data that has become available has allowed us, in particular cases, to rename lineage nomenclature in a biologically more sensible way. Last but not least, updates of the IPD-MHC NHP web site have been scheduled for twice a year, which will provide the scientific community with the most recent available information.

Guidelines for the nomenclature of the non-human primate MHC

Nomenclature for the MHC systems of NHP species

The nomenclature rules for the non-human primate MHCs that were published in 1990 are still up to date. In brief, the *Mhc* symbol is followed by a four-letter abbreviation of the species' scientific name. The first two letters are derived from the name of the genus, and the last two letters from the name of the species. For example, *MhcPatr* defines the MHC system of the common chimpanzee (*Pan troglodytes*). For the sake of convenience, the prefix "*Mhc*" is often omitted after it has been introduced. The symbol is in italics because it defines a genetic system, whereas the abbreviation MHC is retained for general discussions. It is important to note that at present there is no official non-human primate taxonomy. In the nomenclature report of 1990, the scientific names used were based on those listed by Corbet and Hill (Corbet and Hill 1986). At present, the assigning of genus and species level is based on Groves (Groves 2005), and a register of officially accepted MHC symbols for NHP is provided in figure 1. Research in other vertebrate species has resulted in the discovery and description of MHC systems as well, and most have been named according to the nomenclature proposal that was originally published in 1990 (Klein et al. 1990). There is, however, the possibility that the MHCs of different species may be tagged by an identical designation. This committee advises that other research communities publish a register as well, and in such a way that confusion is circumvented as much as possible.

Nomenclature for NHP MHC genes, lineages, and alleles

The hallmark of the MHC system is its unique combination of a high gene density, copy number variation, and an unrivalled high degree of allelic heterogeneity. The HLA system, located within the 6p21.3 region on the short arm of chromosome 6, represents the most thoroughly studied MHC, and the HLA community has a longstanding experience in dealing with nomenclature issues. For that reason, the HLA system has been taken as reference and guide to name MHC factors in NHP species. In the remainder of this report, the rhesus monkey (*Macaca mulatta*) will serve as a reference to illustrate some of the points we wish to make for NHP.

Some HLA loci have been subject to duplication events: for instance, the DQB region, which is occupied in humans by two closely related genes, *HLA-DQB1* and *-DQB2*. There is compelling evidence that humans and Old World monkeys (OWM) share most of the class II loci (Bontrop et al. 1995). Thus, in rhesus monkeys, *Mamu-DQB1* is used to designate the evolutionary ortholog of *HLA-DQB1* (Otting et al. 2002). The ortholog of the *HLA-DQB2* gene is absent in OWM but is present in Great Apes and New World monkeys (NWM) (Bontrop et al. 1995). This example illustrates that in different NHP species, regions of the MHC are subject to expansion and contraction (Bontrop 2006).

Different loci within a gene region are numbered sequentially in the order of description, and for NHP, wherever possible, the HLA system was followed. This was done, for

instance, in the case of the *Mamu-DRB* locus by using the gene names such as *Mamu-DRB1*, *-DRB3*, *-DRB5*, *-DRB6*. However, in some cases in NHP, it is not clear whether we are dealing with different loci or with multiple lineages that belong to the same locus. In these cases, a workshop (W) designation has been introduced. For example, *Mamu-DRB*W1* describes in rhesus monkeys a sequence for which the locus definition is not defined. It is envisaged that many workshop definitions will be dropped in the near future when more haplotype sequencing data become available. Figure 2 provides an overview of the different MHC class II loci described in the HLA system and in the two most intensively studied representatives of Great Apes, OWM, and NWM. Furthermore, extensive gene copy-number variation is described for the classical class I genes in OWM species such as the rhesus monkey (Daza-Vamenta et al. 2004; Otting et al. 2005; Vogel et al. 1999). A comprehensible nomenclature for these loci has recently been introduced, and will be discussed in detail in one of the following sections.

The locus definition is followed by an asterisk and by a two- or three-digit lineage definition. Three-digit lineage definitions are used in those instances in which the lineage number exceeds 99. If lineages are shared between humans and NHP, identical numbers may be used. In practice, this appears to be applicable only to the equivalents of the *HLA-DRB*, *-DQA1*, and *-DQB1* genes (Fig. 3). If lineages are not shared with humans, ascending lineage numbers are introduced so that they do not interfere with the HLA system. For some loci it may be difficult to assign alleles to lineages. In those instances, the discovered alleles are numbered sequentially. This applies to the *DPB* locus, and alleles have been named *Mamu-DPB1*01*, **02*, and so on (Otting et al. 1998), and some non-classical MHC loci (Lawlor et al. 1990; Urvater and Watkins 2000). However, when more data becomes available it may be possible to assign alleles to lineages for these loci as well.

In April 2010, the Nomenclature Committee for the Factors of the HLA system launched a new nomenclature protocol (Marsh et al. 2010). These rules have been followed for the designation of alleles in NHP species, which means that from now on colons will be used to separate lineage and allele designations. For example, *Mamu-DQB1*0602* is now designated as *Mamu-DQB1*06:02*. This approach also facilitates easy recognition of lineages that are characterized by a three-digit definition. The two/three digits after the first colon define the different alleles of a lineage. In general, alleles are named in the order that they are discovered. Allele sharing between different primate species is a rare event (Cooper et al. 1998; Doxiadis et al. 2006), and because alleles are routinely named in the order that they are discovered, it is virtually impossible to give the same lineage-allele definition to alleles that are shared by different species. The introduction of a second colon followed by another two/three digits is applicable when allelic differences at the DNA level are represented by silent/synonymous mutations. Thus, the designations *Mamu-DQB1*06:02:01* and *-DQB1*06:02:02* define two alleles that are identical at the amino acid level but differ for synonymous mutation(s) at the DNA level. Eventually, a third colon and two/three extra digits can be introduced to identify differences in the non-coding region. A summary of how an allele designation is built up is provided (Fig. 4).

Current implemented nomenclature revisions for non-human primates

Adaptations to the macaque *DPB1* locus nomenclature

Variation at the *HLA-DPB1* locus is generated to some extent by point mutations: in addition, however, a frequent exchange of sequence motifs by recombination-like events plays even a more prominent role (Gyllenstein et al. 1996). As a consequence, the *HLA-DPB1* locus is subject to fast evolution, which makes it a challenge to group the different alleles into distinct lineages. This phenomenon is also observed for the *DPB1* locus studied in different non-human primates, and, as discussed previously, alleles discovered for this

locus are numbered sequentially. In particular, rhesus and crab-eating/cynomolgus macaques have been studied extensively in recent years for their *DPBI* locus, and 26 and 57 different alleles have been deposited in the IPD-MHC NHP database, respectively (Aarnink et al. 2011; Creager et al. 2011; Doxiadis et al. 2006; Giraldo-Vela et al. 2008; Hashiba et al. 1993; Ling et al. 2011; O'Connor et al. 2007; Otting et al. 1998; Sano et al. 2006; Slierendregt et al. 1995). As expected, phylogenetic analyses have demonstrated that there is little sharing of *Mhc-DPBI* lineages between humans and NHP. However, extensive sharing is observed between the two macaque species, and the alleles cluster into distinct lineages. Therefore, curators of the IPD-MHC NHP database have adjusted the old macaque *DPBI* nomenclature in a more biologically relevant way (Fig. 5). These nomenclature adaptations became public on the IPD-MHC NHP website with the latest release in March 2012.

Nomenclature modifications for the macaque *Mhc* class I *A* and *B* alleles

Whereas humans have a single copy of the *HLA-A*, *-B*, and *-C* gene per haplotype, the number of these type of class I genes in rhesus monkeys, other OWM, as well as some NWM has been expanded dramatically during evolution (Daza-Vamenta et al. 2004; Kulski et al. 2004; Otting et al. 2005; Shiina et al. 2011). Based on studies involving pedigreed animals, at least seven distinct *A*-like loci have been defined in rhesus monkeys, designated as *Mamu-A1* up to *-A7*, although not all loci are present in each haplotype (Otting et al. 2007). In addition, it needs to be mentioned that the gene products may display differential expression levels and have been grouped into “majors” and “minors” based on transcription level differences (Otting et al. 2005; Rosner et al. 2010; Wiseman et al. 2009). To date, a large number of alleles has been discovered (Boyson et al. 1996; Karl et al. 2008; Loffredo et al. 2007; Miller et al. 1991; Muhl et al. 2002; Otting et al. 2007; Otting et al. 2005; Urvater et al. 2000a; Voss and Letvin 1996; Watanabe et al. 1994; Wu et al. 2008), and been named in a comprehensive manner. For instance, the gene *Mamu-A*01*, which is affiliated with some level of resistance to AIDS induction (Miller et al. 1991; Valentine et al. 2009), is now called *Mamu-A1*001:01*.

The *Mhc-B* region in macaques is even more complex. Sequencing of the complete region in one rhesus monkey has yielded a haplotype that contains 19 distinct paralogous genes, named *Mamu-B1* up to *-B19* (Daza-Vamenta et al. 2004). cDNA sequencing has shown that, at most, nine of these loci are transcribed, but based on differences in level of transcription, it seems that only two or three “majors” are present for each haplotype (Otting et al. 2005; Rosner et al. 2010; Wiseman et al. 2009). Hundreds of *Mamu-B* alleles have been detected, submitted in recent years (Boyson et al. 1996; Karl et al. 2008; Loffredo et al. 2007; Muhl et al. 2002; Otting et al. 2005; Urvater et al. 2000a; Voss and Letvin 1996; Yasutomi et al. 1995), and named thoroughly. For example, *Mamu-B*08*, associated with resistance to SIV infection (Budde et al. 2011; Valentine et al. 2009), is currently designated as *Mamu-B*008:01*. It has been difficult to assign alleles unambiguously to the different *B* loci because the number of *Mamu-B* genes differs between haplotypes due to expansion and contraction processes. For that reason, no locus number designation has been introduced as yet for most *Mamu-B* loci. There are a few exceptions to the rule, however. One oligomorphic locus (*B3*) appears to be present on each haplotype. This locus was earlier described and named *Mamu-I* (Urvater et al. 2000b). Furthermore, sequencing on genomic DNA has yielded alleles of the oligomorphic pseudogenes *Mamu-B11*, *-B12*, *-B16*, *-B17*, and these alleles have been given the respective locus numbers in their designations. Finally, the present nomenclature of the macaque *B* genes uses the old names as lineage designation. If in the future more information becomes available on the gene content of haplotypes, only a locus number designation will need to be introduced.

Finally, phylogenetic analyses of rhesus (*Mamu*), crab-eating (*Mafa*), and southern pig-tailed (*Mane*) macaque *Mhc* class I *A* or *B* alleles have shown extensive intermingling of the

alleles between the three species. The IPD-MHC NHP database curators have recently put considerable effort into streamlining the designations of the macaque *Mhc* class I *A* and *B* alleles (Supplementary Table 1 and 2), in which the rhesus monkey lineage numbers were taken as a leading guide. Thus, *Mamu-A1*001:01* and *Mafa-A1*001:01* define highly related alleles present in two different macaque species. All these adaptations were published at the IPD-MHC NHP website in November 2010 (release version 1.5.0). The nomenclature tables, accessible at the website, list the previous allele designations in the column “Local Names”. Finally, we should strongly emphasize that macaque *A* and *B* lineages are neither related to the lineages in the HLA system nor to those in other non-human primates.

Revisions to the nomenclature for the non-classical class I *E* and *G* loci

In addition to the classical class I loci, the *Mhc* class I region is also occupied by loci designated as non-classicals, which are less polymorphic and may show differential tissue distribution and a specialized function. In humans, these are designated *HLA-E*, *-F*, and *-G* (Marsh et al. 2005). In previous years, researchers were more interested in studying non-classical MHC class I molecules, and a considerable amount of sequence data became available on the *-E*, and *-G* loci of different non-human primate species (Aarnink et al. 2011; Arnaiz-Villena et al. 1997; Boyson et al. 1995; Boyson et al. 1996; Cadavid et al. 1999; Cadavid et al. 1997; Castro et al. 1996; Corell et al. 1994; Knapp et al. 1998; Lafont et al. 2003; Lafont et al. 2004; Lawlor et al. 1990; Mee et al. 2011; Sidebottom et al. 2001; Watkins et al. 1991; Watkins et al. 1990). In the past, the sequences were designated mostly with two digits and numbered based on the order they were detected. A phylogenetic analysis and sequence/amino acid alignment comparison of the *Mhc-E* and *-G* alleles of humans, Great Apes, OWM, and NWM illustrated that the Great Ape sequences are more closely related to the *HLA-E* and *-G* alleles, respectively, and that the OWM and NWM *E* and *G* alleles were more diverse (Fig. 6). Therefore, curators of the IPD-MHC NHP database have again undertaken to match the nomenclature of the *Mhc-E* and *-G* alleles between humans, Great Apes, OWM, and NWM. As can be seen, the Great Ape *E* and *G* alleles were given lineage number 01, as in humans. The OWM *E* and *G* alleles have been given lineage number 02, and the NWM *E* alleles given lineage number 03 (Figs. 6 and 7). For the NWM *G* alleles, more diversification was observed, and the alleles could be grouped into four different lineages, designated 03, 04, 05, and 06 (Figs. 6b and 7b).

The IPD-MHC NHP database

The IPD-MHC NHP database (www.ebi.ac.uk/ipd/mhc/nhp) is a specialized database for the *Mhc* genes and alleles of non-human primate species, first released online in March 2002 (Robinson et al. 2010; Robinson et al. 2003). The database has grown steadily since then (Fig. 8). It is part of the Immuno Polymorphism database (IPD) that comprises data from sources related to the study of polymorphic genes in the immune system. The IPD-MHC NHP database covers Great Apes, OWM, and NWM, and comprises at present almost 4000 sequences divided over several loci of 46 different species (Fig. 9). These comprise currently known and annotated (full-length, or minimal exons 2 and 3) *Mhc* class I sequences, and (full-length, or minimal exon 2) *Mhc* class II sequences, submitted/published by various authors. The team of IPD-MHC NHP curators, with their wide experience in the analyses of diverse NHPs, is responsible for assembling, categorizing, and providing official designations for new alleles. Sequences submitted currently must meet the above-specified criteria, and possess a Genbank/EMBL/DBJ accession number. To enhance the validity of the alleles available at the IPD-MHC NHP database, we encourage the scientific community to submit not only their unreported sequences but also sequences that are identical to already published alleles that have been identified in their studied cohorts. This latter approach will work as an extra quality control system. A BLAST search tool is accessible at the website

for comparing a newly detected sequence with all sequences present in the IPD-MHC NHP database. Additional available features are, for instance, tools for nucleotide or amino acid alignments, a nomenclature tool that shows tables with additional information about a sequence (for example, local name, accession number, and reference), downloads of allelic sets, and a web-based submission tool. The IPD-MHC NHP curators strive to have a database release twice a year, which updates the website with all novel NHP sequences that have become public and/or with other possible updates related to the existing alleles.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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	Species Name		MHC designation	
	Common	Scientific	New	Old
Great Apes	Common Chimpanzee	<i>Pan troglodytes</i>	<i>Patr</i>	<i>ChLA</i>
	Bonobo	<i>Pan paniscus</i>	<i>Papa</i>	
	Lar Gibbon	<i>Hylobates lar</i>	<i>Hyla</i>	
	Western Gorilla	<i>Gorilla gorilla</i>	<i>Gogo</i>	<i>GoLA</i>
	Eastern Gorilla	<i>Gorilla beringei</i>	<i>Gobe</i>	
	Bornean Orangutan	<i>Pongo pygmaeus</i>	<i>Popy</i>	<i>OrLA</i>
	Sumatran Orangutan	<i>Pongo abelii</i>	<i>Poab</i>	
OWM	Blue Monkey	<i>Cercopithecus mitis</i>	<i>Cemi</i>	<i>RhLA</i>
	De Brazza's Monkey	<i>Cercopithecus neglectus</i>	<i>Cene</i>	
	Grivet	<i>Chlorocebus aethiops</i>	<i>Chae</i>	
	Green Monkey	<i>Chlorocebus sabaeus</i>	<i>Chsa</i>	
	Mantled Guereza	<i>Colobus guereza</i>	<i>Cogu</i>	
	Black Crested Mangabey	<i>Lophocebus aterrimus</i>	<i>Loat</i>	
	Stump-tailed Macaque	<i>Macaca arctoides</i>	<i>Maar</i>	
	Crab-eating Macaque #	<i>Macaca fascicularis</i>	<i>Mafa</i>	
	Japanese Macaque	<i>Macaca fuscata</i>	<i>Mafu</i>	
	Rhesus Monkey	<i>Macaca mulatta</i>	<i>Mamu</i>	
	Southern Pig-tailed Macaque	<i>Macaca nemestrina</i>	<i>Mane</i>	
	Lion-tailed Macaque	<i>Macaca silenus</i>	<i>Masi</i>	
	Milne-Edwards's Macaque	<i>Macaca thibetana</i>	<i>Math</i>	
	Drill	<i>Mandrillus leucophaeus</i>	<i>Male</i>	
	Mandrill	<i>Mandrillus sphinx</i>	<i>Masp</i>	
	Olive Baboon	<i>Papio anubis</i>	<i>Paan</i>	<i>Pren</i>
	Yellow Baboon	<i>Papio cynocephalus</i>	<i>Pacy</i>	
	Hamadryas Baboon	<i>Papio hamadryas</i>	<i>Paha</i>	
	Guinea Baboon	<i>Papio papio</i>	<i>Papp</i>	
	Chacma Baboon	<i>Papio ursinus</i>	<i>Paur</i>	
	Northern Plains Grey Langur	<i>Semnopithecus entellus</i>	<i>Seen</i>	
	Gelada	<i>Theropithecus gelada</i>	<i>Thge</i>	
NWM	Azara's Night Monkey	<i>Aotus azarae</i>	<i>Aoaz</i>	<i>OmLA</i>
	Nancy Ma's Night Monkey	<i>Aotus nancymae</i>	<i>Aona</i>	
	Black-headed Night Monkey	<i>Aotus nigriceps</i>	<i>Aoni</i>	
	Three-striped Night Monkey	<i>Aotus trivirgatus</i>	<i>Aotr</i>	
	Spix's Night Monkey	<i>Aotus vociferans</i>	<i>Aovo</i>	
	White-fronted Spider Monkey	<i>Ateles belzebuth</i>	<i>Atbe</i>	<i>MaLA</i> <i>Cepy</i>
	Black-headed Spider Monkey	<i>Ateles fusciceps</i>	<i>Atfu</i>	
	Common Marmoset	<i>Callithrix jacchus</i>	<i>Caja</i>	
	Pygmy Marmoset	<i>Callithrix pygmaea</i>	<i>Capy</i>	
	Red-bellied Titi	<i>Callicebus moloch</i>	<i>Camo</i>	
	Tufted Capuchin	<i>Cebus apella</i>	<i>Ceap</i>	
	Golden Lion Tamarin	<i>Leontopithecus rosalia</i>	<i>Lero</i>	
	White-faced Saki	<i>Pithecia pithecia</i>	<i>Pipi</i>	
	Brown-mantled Tamarin	<i>Saguinus fuscicollis</i>	<i>Safu</i>	
	Geoffroy's Tamarin	<i>Saguinus geoffroyi</i>	<i>Sage</i>	
	White-lipped Tamarin	<i>Saguinus labiatus</i>	<i>Sala</i>	
	Moustached Tamarin	<i>Saguinus mystax</i>	<i>Samy</i>	
	Cottontop Tamarin	<i>Saguinus oedipus</i>	<i>Saoe</i>	
	Common Squirrel Monkey	<i>Saimiri sciureus</i>	<i>Sasc</i>	

		DRA	DRB1	DRB2	DRB3	DRB4	DRB5	DRB6	DRB7	DRB8	DRB9	DRB11	DRB*W	DQA1	DQA2	DQB1	DQB2	DPA1	DPB1
	Human (HLA)	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Great Apes	Chimpanzees (<i>Patr</i>)	+	+	+	+	+	+	+	+	ND	+	-	+	+	+	+	+	+	+
	Gorilla (<i>Gogo</i>)	+	+	?	+	?	+	+	?	?	?	-	+	+	+	+	+	+	+
OWM	Long-tailed macaque (<i>Mafa</i>)	+	+	-	+	+	+	+	-	?	?	-	+	+	-	+	-	+	+
	Rhesus macaque (<i>Mamu</i>)	+	+	-	+	+	+	+	-	?	?	-	+	+	-	+	-	+	+
NWM	Common marmoset (<i>Caja</i>)	ND	+	-	-	-	-	-	-	?	?	-	+	+	?	+	+	+	-
	Cottontop tamarin (<i>Saoe</i>)	ND	+	-	+	-	+	-	-	?	?	+	+	+	?	+	+	ND	+

Fig. 1.
Register of official MHC symbols for non-human primates*

OWM: Old World monkey. NWM: New World monkey. *Designations given in the past, when applicable, are given in the column “MHC designations old”. From the listed species, data is available in the IPD-MHC NHP database. #In the literature this species is often referred to as long-tailed or cynomolgus macaque.

HLA-	<i>Patr-</i>	<i>Mamu-</i>	<i>Caja-</i>
<i>DRB1*03</i>	+	+	+
<i>DRB1*04</i>	- *	+	
<i>DRB1*07</i>	+	+	
<i>DRB1*10</i>	+	+	
<i>DRB3*01</i>	+		
<i>DRB3*02</i>	+		
<i>DRB4*01</i>	+	+	
<i>DRB4*02</i>	+		
<i>DRB5*01</i>	+		
<i>DQA1*01</i>	+	+	+
<i>DQA1*05</i>	+	+	
<i>DQB1*03</i>	+		
<i>DQB1*06</i>	+	+	

Fig. 2.

Overview of the MHC class II loci present in humans and in the two most intensively studied representatives of Great Apes, Old World monkeys (OWM), and New World monkeys (NWM).

Loci are (+) present, (-) absent, (?) not detected, (ND) probably present, no supporting experiments.

Fig. 3.

Overview of the *HLA-DRB*, *-DQA1*, and *-DQB1* lineages shared with three most intensively studied representatives of NHP. The sharing is based on exon 2 sequences (Doxiadis et al. 2008). *The *Patr-DRB1*04* lineage is lost during evolution (de Groot et al. 2009). #The *Caja-DRB1*03* lineage arose via convergent evolution (Antunes et al. 1998).

	Allele designation	Previous designation	Accession number	Ref.
Rhesus Monkey	Mamu- <i>DPB1</i> *01:01	Mamu- <i>DPB1</i> *04	Z32405/EF362435	2/3
	Mamu- <i>DPB1</i> *02:01	Mamu- <i>DPB1</i> *13	Z32410/EU305666	2/4
	Mamu- <i>DPB1</i> *02:02	Mamu- <i>DPB1</i> *24	HM594296	5
	Mamu- <i>DPB1</i> *03:01	Mamu- <i>DPB1</i> *14	AF024563	1
	Mamu- <i>DPB1</i> *03:02	Mamu- <i>DPB1</i> *18	EU363225	4
	Mamu- <i>DPB1</i> *03:03	Mamu- <i>DPB1</i> *20	AB548911	6
	Mamu- <i>DPB1</i> *04:01	Mamu- <i>DPB1</i> *12	Z32409/EU305665	2/4
	Mamu- <i>DPB1</i> *05:01	Mamu- <i>DPB1</i> *03	Z32404/EF426707	2/4
	Mamu- <i>DPB1</i> *06:01	Mamu- <i>DPB1</i> *02	Z32403/EF426705	2/4
	Mamu- <i>DPB1</i> *06:02	Mamu- <i>DPB1</i> *08	Z32415	2
	Mamu- <i>DPB1</i> *06:03	Mamu- <i>DPB1</i> *09	Z32407	2
	Mamu- <i>DPB1</i> *06:04	Mamu- <i>DPB1</i> *11	Z32408	2
	Mamu- <i>DPB1</i> *06:05	Mamu- <i>DPB1</i> *15	AF024564	1
	Mamu- <i>DPB1</i> *07:01	Mamu- <i>DPB1</i> *06	Z32406/EF490966	2/3
	Mamu- <i>DPB1</i> *07:02	Mamu- <i>DPB1</i> *07	Z32412/AF024562	1/2
	Mamu- <i>DPB1</i> *07:03	Mamu- <i>DPB1</i> *23	HM594295	5
	Mamu- <i>DPB1</i> *08:01	Mamu- <i>DPB1</i> *01	Z32402/EF362434	2/3
	Mamu- <i>DPB1</i> *11:01	Mamu- <i>DPB1</i> *16	AF024565	1
	Mamu- <i>DPB1</i> *13:01	Mamu- <i>DPB1</i> *05	Z32413	2
	Mamu- <i>DPB1</i> *14:01	Mamu- <i>DPB1</i> *17	EF544137	3
	Mamu- <i>DPB1</i> *15:01	Mamu- <i>DPB1</i> *10	Z32414/EF362436	2/3
	Mamu- <i>DPB1</i> *16:01	Mamu- <i>DPB1</i> *21	AB548912	6
	Mamu- <i>DPB1</i> *17:01	Mamu- <i>DPB1</i> *22	AB548913	6
	Mamu- <i>DPB1</i> *19:01:01	Mamu- <i>DPB1</i> *190101	EU669872	4
	Mamu- <i>DPB1</i> *19:01:02	Mamu- <i>DPB1</i> *190102	EU934788	4
	Mamu- <i>DPB1</i> *19:02	Mamu- <i>DPB1</i> *1902	EU934787	4
Crab-eating Macaque	Mafa- <i>DPB1</i> *01:01:01	Mafa- <i>DPB1</i> *010101	AB235856/HM580034	8/12
	Mafa- <i>DPB1</i> *01:01:02	Mafa- <i>DPB1</i> *010102	HM580042	12
	Mafa- <i>DPB1</i> *01:02:01	Mafa- <i>DPB1</i> *020101	AB235857/AM086061/HM580036	8/9/12
	Mafa- <i>DPB1</i> *01:02:02	Mafa- <i>DPB1</i> *020102	HM579984	12
	Mafa- <i>DPB1</i> *01:03	Mafa- <i>DPB1</i> *03	AB235858	8
	Mafa- <i>DPB1</i> *01:04	Mafa- <i>DPB1</i> *05	AB235860	8
	Mafa- <i>DPB1</i> *01:05	Mafa- <i>DPB1</i> *06	AB235861/HM579979	8/12
	Mafa- <i>DPB1</i> *01:06	Mafa- <i>DPB1</i> *07	AB235862	8
	Mafa- <i>DPB1</i> *01:07	Mafa- <i>DPB1</i> *09	FR719032	15
	Mafa- <i>DPB1</i> *02:01	Mafa- <i>DPB1</i> *08	AB235863	7
	Mafa- <i>DPB1</i> *02:02	Mafa- <i>DPB1</i> *09	D13335/AB235864/HM580039	7/8/12
	Mafa- <i>DPB1</i> *02:03	Mafa- <i>DPB1</i> *08	D16609	7
	Mafa- <i>DPB1</i> *02:04	Mafa- <i>DPB1</i> *06	HM580040	12
	Mafa- <i>DPB1</i> *02:05	Mafa- <i>DPB1</i> *06	FR719033	15
	Mafa- <i>DPB1</i> *03:01	Mafa- <i>DPB1</i> *10	D13336/AB235865/HM580037	7/8/12
	Mafa- <i>DPB1</i> *03:02	Mafa- <i>DPB1</i> *11	AB235866	8
	Mafa- <i>DPB1</i> *03:03	Mafa- <i>DPB1</i> *12	AB235867/AM086069/EF208812	8/9/10
	Mafa- <i>DPB1</i> *03:04	Mafa- <i>DPB1</i> *07	HM579981	12
	Mafa- <i>DPB1</i> *04:01	Mafa- <i>DPB1</i> *21	AB235876/AM086068/EF208811/HM153019	8/9/10/11
	Mafa- <i>DPB1</i> *05:01	Mafa- <i>DPB1</i> *04	AB235869	8
	Mafa- <i>DPB1</i> *05:02	Mafa- <i>DPB1</i> *01	HM153013/HM579978	11/12
	Mafa- <i>DPB1</i> *06:01	Mafa- <i>DPB1</i> *17	AB235872/HM371252/HM580038	8/11/12
	Mafa- <i>DPB1</i> *06:02	Mafa- <i>DPB1</i> *18	AB235873	8
	Mafa- <i>DPB1</i> *06:03	Mafa- <i>DPB1</i> *19	AB235874/HM153017	8/11
	Mafa- <i>DPB1</i> *06:04	Mafa- <i>DPB1</i> *30	AB235885	8
	Mafa- <i>DPB1</i> *06:05	Mafa- <i>DPB1</i> *31	AB235886	8
	Mafa- <i>DPB1</i> *06:06	Mafa- <i>DPB1</i> *32	AB235887/HM371251/HM579986	8/11/12
	Mafa- <i>DPB1</i> *06:07	Mafa- <i>DPB1</i> *04	HM371247	11
	Mafa- <i>DPB1</i> *06:08	Mafa- <i>DPB1</i> *09	HM579983	12
	Mafa- <i>DPB1</i> *07:01	Mafa- <i>DPB1</i> *20	AB235875/AM086062/HM153016/HM580035/EZ933324	8/9/11/12/13
	Mafa- <i>DPB1</i> *08:01	Mafa- <i>DPB1</i> *23	AB235878	8
	Mafa- <i>DPB1</i> *08:02	Mafa- <i>DPB1</i> *24	AB235879/HM371248	8/11
	Mafa- <i>DPB1</i> *08:03	Mafa- <i>DPB1</i> *25	AB235880/AM086063	8/9
	Mafa- <i>DPB1</i> *08:04	Mafa- <i>DPB1</i> *50	HM153014/AM943635	11/14
	Mafa- <i>DPB1</i> *09:01	Mafa- <i>DPB1</i> *28	AB235883	8
	Mafa- <i>DPB1</i> *09:02	Mafa- <i>DPB1</i> *29	AB235884/EF208813/HM579980	8/10/12
	Mafa- <i>DPB1</i> *09:03	Mafa- <i>DPB1</i> *05	HM371249	11
	Mafa- <i>DPB1</i> *10:01	Mafa- <i>DPB1</i> *22	AB235877/AM086165/HM579982	8/9/12
	Mafa- <i>DPB1</i> *12:01	Mafa- <i>DPB1</i> *26	AB235881	8
	Mafa- <i>DPB1</i> *12:02	Mafa- <i>DPB1</i> *27	AB235882	8
	Mafa- <i>DPB1</i> *15:01	Mafa- <i>DPB1</i> *13	AB235868/HM371245/HM580041	8/11/12
	Mafa- <i>DPB1</i> *15:02	Mafa- <i>DPB1</i> *14	AB235869/AM086066/HM579977/EZ933323	8/9/12/13
	Mafa- <i>DPB1</i> *15:03	Mafa- <i>DPB1</i> *15	AB235870/AM086067/AM943636	8/9/14
	Mafa- <i>DPB1</i> *15:04	Mafa- <i>DPB1</i> *16	AB235871/AM943634	8/14
	Mafa- <i>DPB1</i> *15:05	Mafa- <i>DPB1</i> *44	AM086064/HM371250/FR719031	9/11/15
	Mafa- <i>DPB1</i> *15:06	Mafa- <i>DPB1</i> *45	AM086065/HM579985	9/12
	Mafa- <i>DPB1</i> *15:07	Mafa- <i>DPB1</i> *52	HM371244	11
	Mafa- <i>DPB1</i> *17:01	Mafa- <i>DPB1</i> *53	HM371246	11
	Mafa- <i>DPB1</i> *18:01	Mafa- <i>DPB1</i> *34	AB235889	8
	Mafa- <i>DPB1</i> *18:02	Mafa- <i>DPB1</i> *41	AB235896	8
	Mafa- <i>DPB1</i> *19:01	Mafa- <i>DPB1</i> *35	AB235890/HM153018	8/11
	Mafa- <i>DPB1</i> *19:02	Mafa- <i>DPB1</i> *36	AB235891	8
	Mafa- <i>DPB1</i> *19:03	Mafa- <i>DPB1</i> *37	AB235892/EF208814	8/10
	Mafa- <i>DPB1</i> *19:04	Mafa- <i>DPB1</i> *38	AB235893	8
	Mafa- <i>DPB1</i> *19:05	Mafa- <i>DPB1</i> *39	AB235894	8
	Mafa- <i>DPB1</i> *19:06	Mafa- <i>DPB1</i> *40	AB235895/HM153015	8/11
	Mafa- <i>DPB1</i> *20:01	Mafa- <i>DPB1</i> *43	EF208815	10

Fig. 4.
Illustration of how a designation for a NHP MHC allele is accomplished

Fig. 5.

Rhesus and crab-eating/cynomolgus macaque *DPB1* allele designations Ref.: reference.

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Fig. 6. Phylogenetic analysis of *Mhc-E* and *-G* alleles of humans, Great Apes, Old World monkeys (OWM), and New World monkeys (NWM). **a** *Mhc-E*. **b** *Mhc-G*. Brackets illustrate the division into different lineages. *Based on sequence/amino acid alignment comparison this allele is designated to lineage 03.

a	Allele designation	Previous designation	Accession number	Ref.
Great Apes	<i>Gogo-E*01:01:01</i>	<i>Gogo-E*01</i>	L77737	8
	<i>Gogo-E*01:01:02</i>	<i>Gogo-E*02</i>	L77736	8
	<i>Patr-E*01:01:01:01</i>	<i>Patr-E*01</i>	L77735	8
	<i>Patr-E*01:01:01:02</i>	<i>Patr-E*02</i>	L77074	8
	<i>Popy-E*01:01</i>	<i>Popy-E*01</i>	M30681	1
OWM	<i>Mafa-E*02:01</i>	<i>Mafa-E*01</i>	U02976	5
	<i>Mafa-E*02:02</i>	<i>Mafa-E*02</i>	U02977	5
	<i>Mafa-E*02:03</i>		EZ933311	18
	<i>Mafa-E*02:04</i>		EZ933312	18
	<i>Mafa-E*02:05N</i>		HP823080	18
	<i>Mamu-E*02:01:01</i>	<i>Mamu-E*010101</i>	U02978	5
	<i>Mamu-E*02:01:02</i>	<i>Mamu-E*010102</i>	EF372279, EU934770	14
	<i>Mamu-E*02:02</i>	<i>Mamu-E*0102</i>	U02979/FM986653	5/15
	<i>Mamu-E*02:03</i>	<i>Mamu-E*0103</i>	U02980/EF611171	5/14
	<i>Mamu-E*02:04</i>	<i>Mamu-E*0104</i>	U02981/EU305662	5/14
	<i>Mamu-E*02:05</i>	<i>Mamu-E*0105</i>	U41837	6
	<i>Mamu-E*02:06</i>	<i>Mamu-E*0106</i>	L41822	8
	<i>Mamu-E*02:07</i>	<i>Mamu-E*0107</i>	EF611170	14
	<i>Mamu-E*02:08</i>	<i>Mamu-E*0108</i>	L41824	8
	<i>Mamu-E*02:09</i>	<i>Mamu-E*0109</i>	EF611169	14
	<i>Mamu-E*02:10</i>	<i>Mamu-E*0110</i>	EU109710.	14
	<i>Mamu-E*02:11</i>	<i>Mamu-E*0111</i>	EU109711	14
	<i>Mamu-E*02:12:01</i>	<i>Mamu-E*011201</i>	EU305658	14
	<i>Mamu-E*02:12:02</i>	<i>Mamu-E*011202</i>	GQ471889	14
	<i>Mamu-E*02:13</i>	<i>Mamu-E*0113</i>	EU305659	14
	<i>Mamu-E*02:14</i>	<i>Mamu-E*0114</i>	EU305660	14
	<i>Mamu-E*02:15</i>	<i>Mamu-E*0115</i>	EU305661	14
	<i>Mamu-E*02:16</i>	<i>Mamu-E*0116</i>	EU934771	14
	<i>Mamu-E*02:17</i>	<i>Mamu-E*0117</i>	FJ544410	14
	<i>Mamu-E*02:18</i>	<i>Mamu-E*0118</i>	GQ471890	14
	<i>Mamu-E*02:19</i>	<i>Mamu-E*0119</i>	L41823/HM106999	8/16
	<i>Mamu-E*02:20</i>	<i>Mamu-E*0201</i>	EU109709	14
	<i>Mane-E*02:01</i>	<i>Mane-E*0101</i>	AY204714	13
	<i>Mane-E*02:02</i>	<i>Mane-E*0102</i>	AY204717	13
	<i>Mane-E*02:03</i>	<i>Mane-E*0103</i>	AY204718	13
	<i>Mane-E*02:04</i>	<i>Mane-E*0201</i>	AY204719	13
	<i>Mane-E*02:05</i>	<i>Mane-E*0202</i>	AY204720	13
	<i>Mane-E*02:06</i>	<i>Mane-E*0301</i>	AY204713	13
	<i>Mane-E*02:07</i>	<i>Mane-E*0401</i>	AY204721	13
	<i>Mane-E*02:08</i>	<i>Mane-E*0501</i>	AY204722	13
	<i>Pacy-E*02:01</i>	<i>Pacy-E*01</i>	AF288706	12
NWM	<i>Aotr-E*03:01</i>	<i>Aotr-E*01</i>	AF004921	10
	<i>Atbe-E*03:01</i>	<i>Atbe-E*01</i>	AF004923	10
	<i>Atfu-E*03:01</i>	<i>Atfu-E*01</i>	AF004924	10
	<i>Atfu-E*03:02</i>	<i>Atfu-E*02</i>	AF004925	10
	<i>Caja-E*03:01</i>	<i>Caja-E*01</i>	AF004919	10
	<i>Caja-E*03:02</i>	<i>Caja-E*02</i>	AF004920	10
	<i>Pipi-E*03:01</i>	<i>Pipi-E*01</i>	AF004922	10
	<i>Saoe-E*03:01</i>	<i>Saoe-E*01</i>	AF004918	10

b	Allele designation	Previous designation	Accession number	Ref.
Great Apes	Gogo-G*01:01	Gogo-G*01, Gogo-G*1	M95736	4
	Papa-G*01:01	Papa-G*01, Papa-G*1	U33289	8
	Patr-G*01:01	Patr-G*01, Patr-G*1	M95737	4
OWM	Chae-G*02:01	Ceae-G*01, Ceae-G*1	U33310	7
	Chae-G*02:02	Ceae-G*02, Ceae-G*11	U33311	7
	Mafa-G*02:01	Mafa-G*01	U33312	7
	Mafa-G*02:02	Mafa-G*02	U33301	7
	Mafa-G*02:03	Mafa-G*03	U33302	7
	Mafa-G*02:04	Mafa-G*04	U33303	7
	Mamu-G*02:01	Mamu-G*01	U33304	7
	Mamu-G*02:02	Mamu-G*02	U33305	7
	Mamu-G*02:03	Mamu-G*03	U33306	7
	Mamu-G*02:04	Mamu-G*04	U33295	7
NWM	Aotr-G*03:01	Aotr-G*01	U59644	9
	Aotr-G*05:01	Aotr-G*02	U59645	9
	Aotr-G*05:02	Aotr-G*03	U59646	9
	Atbe-G*03:01	Atbe-G*01	U59647	9
	Atbe-G*03:02	Atbe-G*03	U59650	9
	Atbe-G*06:01	Atbe-G*02	U59649	9
	Caja-G*03:01	Caja-G*01	U59637	9
	Caja-G*03:02	Caja-G*02	U59638	9
	Caja-G*03:03	Caja-G*03	U59639	9
	Caja-G*03:04	Caja-G*04	U59640	9
	Caja-G*03:05	Caja-G*05	U59641	9
	Lero-G*03:01	Lero-G*01	U59642	9
	Lero-G*03:02	Lero-G*02	U59643	9
	Pipi-G*03:01	Pipi-G*01	U59651	9
	Pipi-G*03:02	Pipi-G*02	U59652	9
	Pipi-G*03:03	Pipi-G*05	U59656	9
	Pipi-G*04:01	Pipi-G*03	U59653	9
	Safu-G*03:01	Safu-G*01	U59633	9
	Safu-G*03:02	Safu-G*02	U59634	9
	Safu-G*03:03	Safu-G*03	U59635	9
	Safu-G*03:04	Safu-G*04	U59636	9
	Sala-G*03:01		JF785553	17
	Sala-G*03:02		JF785554	17
	Sala-G*03:03		JF785555	17
	Sala-G*03:04		JF785556	17
	Sala-G*03:05		JF785560	17
	Sala-G*03:06		JF785561	17
	Sala-G*03:07		JF785562	17
	Sala-G*03:08		JF785564	17
	Sala-G*03:09N		JF785557	17
	Sala-G*03:10N		JF785558	17
	Sala-G*03:11N		JF785559	17
	Sala-G*03:12N		JF785563	17
	Sala-G*03:13N		JF785565	17
	Saoe-G*03:01	Saoe-G*01, So-4	M38405/M63946	3/8
	Saoe-G*03:02	Saoe-G*02, So-5	M38412/M63953	3/8
	Saoe-G*03:03	Saoe-G*03, So-6	M38409/M63950	3/8
	Saoe-G*03:04	Saoe-G*04, So-8	M38406/M63947	3/8
	Saoe-G*03:05	Saoe-G*05, So-16	U49331	3
	Saoe-G*03:06	Saoe-G*06, So-17	M38407/M63948	3/8
	Saoe-G*03:07	Saoe-G*07, So-21	M38403/M63944	3/8
	Saoe-G*03:08	Saoe-G*08, So-24	M38408/M63947	3/8
	Saoe-G*03:09	Saoe-G*09, So-32	M38410/M63951	3/8
	Saoe-G*03:10	Saoe-G*10, So-46	M38411/M63952	3/8
	Saoe-G*03:11	Saoe-G*11, So-47	M38413/M63954	3/8
	Saoe-G*03:12 Ps	Saoe-G*12 Ps	AF020686	11
	Saoe-G*03:13 Ps	Saoe-G*13 Ps	AF020687	11
	Saoe-G*03:14 Ps	Saoe-G*14 Ps	AF020688	11
	Saoe-G*03:16 Ps	Saoe-G*16 Ps	AF020690	11
	Saoe-G*03:17 Ps	Saoe-G*17 Ps	AF020691	11
	Saoe-G*03:18 Ps	Saoe-G*18 Ps	AF020692	11
	Saoe-G*03:19 Ps	Saoe-G*19 Ps	AF020693	11
	Saoe-G*03:20 Ps	Saoe-G*20 Ps	AF020694	11
	Sasc-G*04:01	Sasc-G*02	U59658	2

Fig. 7. Great Apes, Old World monkeys (OWM), and New World monkeys (NWM) *E* and *G* allele designations. **a** *Mhc-E*. **b** *Mhc-G*.

N means null allele; allele is characterized by a premature stopcodon. *Ps* was used by Cadavid et al. to indicate that the alleles are pseudogenes: we have used the same abbreviation in the new designations. Ref.: reference.

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Fig. 8.
Annual growth of the IPD-MHC NHP database

	Common species name	No. of alleles	Loci for which data is present																
			Class I			Class II						Non classical							
			A	B	C	DP	DQ	DR	DM	DO	AL	E	F	G	AG	H	I	N	P
Great Apes	Common Chimpanzee	266	+	+	+	+	+	+	+	+	+	+	+	+	+				
	Bonobo	30	+	+	+														
	Lar Gibbon	13	+	+															
	Gorilla (Gogo)	82	+	+	+	+	+	+	+				+				+		
	Orangutan (<i>Popy</i>)	50	+	+	+	+	+	+	+									+	
OWM	Blue Monkey	8							+										
	De Brazza's Monkey	2							+										
	Grivet	29	+	+					+						+	+			
	Green Monkey	25	+	+															
	Mantled Guereza	1							+										
	Black Crested Mangabey	1							+										
	Stump-tailed Macaque	15							+	+	+							+	
	Crab-eating Macaque	1344	+	+		+	+	+	+		+			+	+	+		+	
	Japanese Macaque	27							+										
	Rhesus Monkey	1096	+	+		+	+	+	+		+	+	+	+	+			+	
	Southern Pig-tailed Macaque	408	+	+		+	+	+			+			+	+			+	
	Lion-tailed Macaque	9							+										
	Milne-Edwards's Macaque	37							+	+									
	Drill	2																	
	Mandrill	42																	
	Olive Baboon	11	+	+					+								+		
	Yellow Baboon	18	+	+					+										
	Hamadryas Baboon	9				+	+	+	+		+								
	Guinea Baboon	4							+										
Chacma Baboon	23																		
Northern Plains Grey Langur	1							+											
Gelada	2							+											
NWM	Azara's Night Monkey	2							+										
	Nancy Ma's Night Monkey	122							+	+	+								
	Black-headed Night Monkey	32							+	+	+								
	Three-striped Night Monkey	17							+	+	+				+			+	
	Spix's Night Monkey	12																	
	White-fronted Spider Monkey	8							+					+	+				
	Black-headed Spider Monkey	2												+	+				
	Common Marmoset	61				+			+	+				+	+			+	
	Pygmy Marmoset	2							+										
	Red-bellied Titi	15							+										
	Tufted Capuchin	6							+										
	Golden Lion Tamarin	2													+				
	White-faced Saki	9				+			+				+	+					
	Brown-mantled Tamarin	6												+				+	
	Geoffroy's Tamarin	2																+	
	White-lipped Tamarin	19							+					+					
	Moustached Tamarin	2																+	
	Cottontop Tamarin	79				+	+	+				+	+	+				+	
	Common Squirrel Monkey	15				+	+	+											

Fig. 9.

Overview of the data that is available at the IPD-MHC NHP website. The table provides the number (No.) of alleles present per species, and for which loci data are present on the website (indicated with a +). OWM: Old World monkey. NWM: New World monkey.