The hidden benefits of sex: evidence for MHC-associated mate choice in primate societies

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ABSTRACT (SUMMARY)

Major Histocompatibility Complex (MHC)-associated mate choice is thought to give offspring a fitness advantage through disease resistance. Primates offer a unique opportunity to understand MHC-associated mate choice within our own zoological order, while their social diversity provides an exceptional setting to examine the genetic determinants and consequences of mate choice in animal societies. Although mate choice is constrained by social context, increasing evidence shows that MHC-dependent mate choice occurs across the order in a variety of socio-sexual systems and favours mates with dissimilar, diverse or specific genotypes non-exclusively. Recent research has also identified phenotypic indicators of MHC quality. Moreover, novel findings rehabilitate the importance of olfactory cues in signalling MHC genes and influencing primate mating decisions. These findings underline the importance to females of selecting a sexual partner of high genetic quality, as well as the generality of the role of MHC genes in sexual selection.

INTRODUCTION

Darwin's theory of inter-sexual selection, or mate choice[1], has been the subject of a proliferation of studies over the past few decades[2,3]. A key question is how to explain mate choice where the choosy sex (usually the female) receives few or no direct benefits, in the form of resources or parental care, from the chosen sex (usually the male). In such cases, females are thought to obtain indirect, genetic, benefits from their partner[2]. In line with this, increasing evidence suggests that the MHC influences mate choice in vertebrates[4,5]. MHC genes encode cell-surface glycoproteins which play a critical role in the immune system by recognising foreign peptides, presenting them to specialised immune cells and initiating the appropriate immune response[6]. The extensive population-level allelic diversity of the MHC[7] is thought to be maintained by pathogen-driven balancing selection, materno-foetal interactions and sexual selection[8]. MHC-associated mate choice can take three forms, yielding different advantages for the chooser and resulting offspring[9,10]:

- Choice for a good combination of genes in the offspring[11] (Hypothesis 1). This often takes the form of choice for genetic dissimilarity (disassortative mating) or complementarity. Such choice may serve to avoid potential deleterious fitness effects of inbreeding by increasing genome-wide genetic diversity, or may increase MHC diversity in offspring. Since MHC genes are expressed co-dominantly, increased MHC diversity (defined as the number of distinct MHC alleles at particular MHC loci) is thought to give individuals the ability to recognise and react to a broader range of pathogens, ('heterozygote advantage', where heterozygosity refers to the number of MHC haplotypes, which constitute blocks of linked sequences with Mendelian inheritance, and generally correlates with diversity)[12]. Alternatively, a fitness advantage in individuals possessing intermediate (rather than maximum) MHC diversity may favour choice for an optimally dissimilar partner ('allele counting')[13,14]. In all these cases, mate choice is not biased towards one particular ideal mate, but dependent on the chooser's genotype.
- Choice for an MHC-diverse mate (Hypothesis 2). In theory, individuals are unable to pass on heterozygosity at specific loci. However, heterozygote males possess more

rare alleles than homozygous mates on average, thus potentially produce offspring with rarer MHC genotypes and higher heterozygosity than homozygotes[8]. In this case, mate choice converges on the same lucky individuals.

- Choice for individuals that possess particular MHC genotypes (Hypothesis 3). Particular alleles may be beneficial when rare, but disadvantageous when common, because natural selection favours parasites that can evade the MHC-dependent immunity of the most common host genotypes, decreasing the fitness of individuals possessing common alleles[8]. Under this model, mate choice also converges on particular individuals possessing the desired genotype, amplifying or accelerating the effects of natural selection favouring host adaptation to constantly moving antigenic targets.

Here we review recent evidence from the first studies to investigate MHC-associated mate choice in non-human primates. First, we outline why primates are of particular interest in the context of mate choice. Next we review the results of existing studies, asking whether simple social or environmental differences provide a general interpretative framework for the variation in mate choice outcomes observed across the order. We then review a variety of findings that point to new perspectives concerning how primates might identify their most suitable mating partner. We end by envisioning technological improvements which should foster progress in understanding the role of MHC in mating decisions in primate societies. Throughout, we identify relevant research trends and gaps in the wider fields of MHC-biology and primatology. While MHC-correlated mate choice in humans has been thoroughly reviewed recently[15,16], and is beyond the scope of this review, we emphasise how non-human primate research might shed light on human behaviour, and vice versa, where relevant.

WHY PRIMATES?

The approximately 400 species in the order Primates include the one extant species of human (*Homo sapiens*). In contrast to the diversity of MHC organisations reported for non-

mammals, MHC architecture is very similar in human and non-human primates[17], comprising a large gene cluster typically divided into class I and II regions. Class I genes are expressed on almost all nucleated cells and act in defense against intracellular (mainly viral) pathogens, while class II genes are expressed on immune cells and involved in detecting antigens (mainly bacterial and parasitic) from the extracellular environment[17]. Within regions, species differ in the number, organisation, sequence and allelic diversity of MHC genes[18], but long-term retention of allelic lineages within the primate order reflects shared evolutionary history combined with vulnerability to similar pathogenic pressures[18].

A key to understanding human mate choice

Humans are presented as an ideal model species for understanding the complex role of MHC in mate choice[16]. Experiments or surveys can be conducted easily, facilitating studies of mate preference[15,16]. [Mate 'preference' describes how individuals evaluate prospective mates, while 'choice' is the behavioural manifestation of preference, and is influenced by a number of external factors, such as demography (pool of available partners) or mating strategies of the other sex[19]. According to this definition, documenting mate choice requires direct observations of mating, or deduction of mating outcomes via genotyping]. Moreover, studies of mating outcomes in humans span large MHC regions, sometimes in thousands of couples[15,16], due to the rich information available for the human MHC (known as human leukocyte antigen, HLA). In this context, can non-human studies really contribute to our understanding of the evolution of MHC-correlated mate choice in humans? We believe they can, for several reasons.

Full understanding of the evolution of a trait requires: (1) tracking its evolutionary trajectory, which means documenting its presence and form in related species, (2) studying the selective pressures that have favoured its emergence and maintenance (e.g. local parasite communities in the case of MHC-associated mate choice). In the first case, it is obvious that studying non-human primates can help to trace the evolutionary history of

human behaviour, given their phylogenetic proximity. In the second, studying non-primates might palliate difficulties faced in studies of human behaviour. Due to large-scale migrations and profound lifestyle changes during our recent past, there is often a major gap between the ecological and social environments of ancient and contemporary humans. Among other factors, modern human populations can be composed of different ethnic groups, where assortative or disassortative patterns of mating with respect to MHC genes may constitute artefacts induced by the genetic structure of the population, such as culturally-reinforced assortative mating within subgroups[15]. In contrast, studies of non-human primates target homogeneous populations, which (at least for studies focusing on natural populations) are likely to have evolved in their contemporary environment.

The study of MHC-associated mate choice and its evolutionary consequences in humans poses additional methodological challenges which do not apply to studies of non-human primates. First, while it is easy to study mate preference, it is impossible to observe mating behaviour in humans. Behavioural studies of human mate choice are thus largely based on questionnaires[15,16], which do not necessarily represent reliable approximations of behaviour. Human mating decisions can also be deduced from marriage patterns, but choice of marriage (i.e., social) partners may be socially constrained, and may differ from sexual partners due to extra-pair copulations. In contrast, many non-human primate studies include routine monitoring of sexual behaviour, in some cases over decades, in parallel with genetic paternity data. Moreover, studies of non-humans can examine questions that are typically difficult to address in humans, such as the genetic differences between social and extra-pair mates in pair-living species. Likewise, it is difficult to measure the actual benefits of mate choice in humans, although such information is crucial to our understanding of the evolutionary determinants of mate choice. The fitness consequences of choices are typically easier to estimate in primate populations for which long-term data are available, by comparing individual fitness-related measures such as survival, longevity or reproductive success in offspring born to different combinations of partners.

Non-human primates are of interest in their own right

A number of unique characteristics make primates interesting candidates for the study of MHC-associated mate choice in their own right. Primates exhibit broad socio-ecological diversity, including solitary, pair-living and group-living taxa, in which males, females or both sexes disperse, with different types of parental care, and monogamous, polyandrous, polgynous and polygynandrous mating patterns[20]. This diversity suggests that the expression of mate choice and reproductive strategies, which are highly conditional on the socio-sexual system, may vary to the same extent[21]. For example, group members typically know one other as individuals in social species, allowing cumulative mate assessment over time, in contrast to the rapid choice made by seasonally pairing birds, for example[21]. Moreover, group size, social structure and dominance hierarchies may further constrain individual mating strategies. For example, reproduction may be largely monopolised by top-ranking males in mixed sex groups[22]. Primate studies thus help us to resolve important questions regarding the evolution of mate choice in animal societies, such as whether mate preferences for good genes can evolve in a social context, and how individual preferences translate into choices in spite of social constraints.

Beyond the individual, the mating system is a major determinant of population genetic structure, which is, in turn, expected to shape individual mating strategies over an evolutionary time-frame. Studying MHC-associated mate choice across the primate order will improve our understanding of gene dynamics in social systems, including questions of how genetic diversity is partitioned among social units, and the behavioural consequences of this partitioning[23]. Both theoretical and empirical attempts to address such questions are currently missing in the context of functional genetic variation.

Finally, and crucially, primates are popular study species, and detailed information is available concerning their behaviour and ecology, providing a rich source of comparative data. Existing studies of MHC-associated mate choice in primates, while still relatively few, represent the greatest number of species studied within any vertebrate order, offering new perspectives for comparative discussions.

So, what do primates choose? (Hint: it depends)

We summarise the five studies of the relationship between MHC genotype and patterns of reproduction in non-human primates that have been published so far, including two lemurs (strepsirrhines) and three Old World monkeys (cercopithecines), in Table 1. Despite concentrating on small sections of the MHC, studies of mating outcome provide some support for all three forms of MHC-associated mate choice. They suggest that MHC-dependent mate choice is widespread across the order, including diverse social and mating systems, and that such choice can be expressed in group-living species, despite the tight control exerted by males over reproductive opportunities.

Choice for MHC dissimilarity (Hypothesis 1)

Selection for maximal (but not optimal) MHC dissimilarity occurs in both pair-living and solitary, promiscuous nocturnal lemurs, and mandrills, a polygynandrous, diurnal species that lives in large groups with high levels of male-male competition (Table 1). However, studies of macaques and baboons found no link between mating outcome and MHC dissimilarity. Studies of partner choice in relation to MHC in humans report similar mixed results, with biases for MHC-similarity, MHC-dissimilarity, or no significant departure from random. Recent reviews conclude that these conflicting patterns may reflect methodological differences, or context-dependent mate preferences linked to the genetic structure of study populations[15,16]. In particular, mate choice for MHC-dissimilarity has been detected in isolated and relatively inbred populations[24,25], but not in outbred populations[24,26,27]. The contrasting results obtained from studies of closely related mandrills and baboons suggest a similar pattern in non-human primates. The mandrill colony is an isolated, relatively inbred, population[28], whereas free dispersal among genetically differentiated groups favours high levels of outbreeding in the wild baboon population. Together, these results support the idea that a mating strategy favouring the

production of outbred offspring is especially important in relatively isolated populations, or where there is less heterogeneity in other factors influencing mate choice.

Choice for MHC diversity (Hypothesis 2)

Selection for MHC diverse males occurs in all species studied except baboons (Table 1). Selection also occurs for genome-wide diversity in mandrills and lemurs, although not in macaques. In lemurs and mandrills this is associated with choice for MHC dissimilarity, which may reflect non-independence between estimators of individual heterozygosity and pairwise dissimilarity[29]. Future studies should use estimators of dissimilarity that control for individual diversity[30,31] to disentangle these two strategies, because individuals possessing many MHC alleles are expected to share, on average, a higher number of different sequences with any randomly chosen partner than individuals with low diversity under high levels of allelic diversity.

Choice for particular genotypes (Hypothesis 3)

Identifying mate choice for particular genotypes necessitates a large sample size, particularly since advantageous alleles are likely to be rare[32]. Thus it is not surprising that direct evidence for such a strategy is relatively weak so far. However, suggestive findings are available for fat-tailed dwarf lemurs, where males possessing specific MHC class II supertypes – groups of MHC sequences that share peptide-binding motifs and are therefore thought to be functionally similar – have a reproductive advantage[33]. Moreover, female baboons possessing a particular, common MHC supertype display smaller sexual swellings than others[34], while males prefer females with large swellings in this population[35]. Similarly, intense red facial coloration is associated with the possession of particular MHC supertypes in male mandrills[37], and is favoured by females[36]. Thus both female and male ornaments may act as signals of 'good genes' to the opposite sex.

There are no global patterns

At first sight, it is difficult to detect a global pattern across the order, as the targets of mating decisions are not necessarily consistent among the few species examined so far. Although this might seem preliminary or contradictory – and even disappointing – it underlines two important points. First, the targets of MHC-associated mate choice are not mutually exclusive, and different choice strategies (e.g., targeting dissimilar or particular genotypes) can coexist in a given population at a given time. Second, and perhaps most importantly, we probably should not expect any one simple trend. Current evidence suggests context-dependence and possibly even intra-specific flexibility in targeting partners[15], suggesting that we should expect a patchwork of locally coherent schemes instead. As a result, concentrating research efforts on well-known study systems, using integrative approaches that investigate behavioural patterns in relation to their wider genetic and ecological context, may prove more insightful than accumulating snapshot descriptions of mating patterns in new species.

How do primates identify their ideal mate?

Choosing for dissimilar genes (Hypothesis 1): Sex and the sniffy?

In some cases mate choice for MHC-dissimilarity may simply reflect classical inbreeding avoidance, based on cues that are not necessarily MHC-associated. For example, in mandrills, the influence of MHC dissimilarity on a male's probability of conceiving offspring was no longer significant when excluding the most related dyads from the analysis, suggesting that mandrills might 'simply' avoid mating with relatives. If so, we need to understand how they discriminate kin. Recognition of familiar kin is typically credited to social learning, through stable bonds created during early development[38]. Identification of unfamiliar kin (such as paternal relatives when paternity uncertainty is high) may rely on alternative mechanisms, including self-referent phenotype matching – the comparison

between own and other's phenotype[39]. Many cues reflect relatedness in non-human primates, including visual appearance[40], vocalisations[41] and odours[42,43] and exciting new findings suggest that both human[44] and non-human primates[45] may use such cues in kin discrimination.

Some evidence suggests that choice for MHC dissimilarity may not simply result from inbreeding avoidance based on alternative cues (due to correlations between MHC and genome-wide dissimilarity). First, detailed statistical analyses in the lemur and mandrill studies suggest that MHC dissimilarity predicts mating patterns slightly better than genome-wide relatedness (Table 1). Moreover, experiments on rodents suggest that olfactory perception of MHC-similarity occurs beyond the perception of relatedness[46,47]. Although the physiological pathways linking MHC genes to odour production remain undefined[47], these findings suggest fine-scale perception of MHC genotype. A functional link between MHC and olfactory communication is further supported by the tight genomic linkage between MHC and olfactory receptor genes in humans and rodents[48], and the activation of vomeronasal receptors (involved in the detection of pheromones) by MHC class I derived peptides in rodents[49]. Thus it appears plausible that inbreeding avoidance genuinely relies on MHC-associated cues, rather than incidentally resulting in MHC-biased mate choice.

Monkeys and apes have traditionally been considered as 'microsmatic'[50], and olfactory cues have thus been thought less important than visual ones in their mating decisions[51]. This view is based largely on molecular data showing a decline in the number of functional olfactory receptors in parallel with the emergence of trichromatic vision after the divergence between New and Old World monkeys[52], accompanied by deterioration of the vomeronasal pheromone transduction pathways in anthropoids[51]. However, new molecular evidence challenges this, and even suggests that the olfactory receptor gene repertoire in humans is more similar to that of marmosets than those of orangutans or macaques[53]. In parallel, a resurgence of interest in primate olfactory capacities provides further support for the idea that chemical cues play a role in communication in all major primate radiations[50,54,55]. Analysis of the content of chemical signals suggest that they can

advertise individual traits in ring-tailed lemurs[43], mandrills [56] and humans[57]. Moreover, odour signals genome-wide diversity and genetic relatedness in ring-tailed lemurs[43,58] and mandrills[59], plus MHC diversity and dissimilarity in mandrills[59]. A final piece of evidence arises from the famous 'sweaty T-shirt' experiments in humans, which complement correlative designs in non-human primates by showing that MHC-associated olfactory cues are perceived, and may even influence mating preferences[15,16].

Choosing for diversity or for particular genes (Hypotheses 2 & 3): Conspicuous displays

Evidence for selection for MHC-diversity or for particular genotypes suggests that phenotypic cues convey information regarding genotype to the chooser. Obvious candidates here are the striking displays exhibited by primates of both sexes, including visual (e.g., bright colours and ornaments), acoustic (e.g., long calls) and olfactory advertisement[60]. According to 'good genes' paradigms, such costly secondary sexual characters attract mates by signaling heritable genetic quality[61,62]. Myriad studies link ornament expression to fitness-related traits in non-primates[2,3], but the 'good genes' behind ornamentation have rarely been identified; MHC genes represent obvious candidates due to their role in disease resistance[4]. Primate displays advertise status in males[37] and reproductive quality in females[35,63] and primates might further use these ornaments to choose partners with intrinsic genetic quality, such as high MHC diversity or advantageous MHC genotypes. In line with this, some of the most emblematic primate ornaments, the red coloration of mandrills and the size and morphology of baboon sexual swellings, signal the possession of specific MHC class II supertypes[37,34] (Fig. 2). Although humans lack such colourful displays, women find the odour of MHC-diverse males more attractive than that of less diverse males[64] and faces of MHC-heterozygote males more attractive than those of homozygotes[65,66], suggesting that similar mechanisms exist in humans.

Choosing after sex: sperm-sorting and other post-mating processes (all hypotheses)

Despite intriguing indirect support, there is no formal evidence that MHC-dependent choice occurs prior to copulation in either humans or non-human primates. Moreover, promiscuity probably partially reflects primate females' difficulty in expressing free pre-copulatory choice[67]. However, post-copulatory mechanisms also potentially mediate MHC-biased reproduction in primates. For example, reduced heterozygosity impairs sperm quality[68] and may be a disadvantage in sperm competition. Cryptic female choice for sperm with complementary genes may lead to selective fertilisation, implantation or abortion[69]. Whether MHC haplotype is expressed on the surface of mature spermatozoids, and can be detected by the female, is controversial[70]. However, there is good evidence for the expression of the MHC-linked olfactory receptor genes on spermatozoa in both mice and humans[71]. Because these molecules serve as guidance cues[71], they may adjust sperm motility selectively in response to individual chemical cues in the female reproductive tract[72]. Moreover, mouse fertilisation is non-random with respect to parental MHC genotypes[73], which may promote postcopulatory inbreeding avoidance[74]. Complex immune reactions mediating the maternal tolerance of the trophoblast may contribute extra MHC-dependent selective steps in mammals, including primates[75]. Placental expression of foetal MHC class I molecules has been detected in several primate species[76]. These molecules, partially encoded by the paternal haplotype, may represent 'non-self' for the mother but nevertheless contribute to the regulation of the maternal immune response throughout gestation[77]. Consequently, post-insemination MHC-dependent selection may be of particular importance in primates, and account for the higher probability of pregnancy failure reported for couples displaying above-average MHC similarity in humans[78] and macaques[79].

Postcopulatory selection has attracted less attention than precopulatory selection in primates due to the difficulty of hypothesis testing. Correlative studies typically require accurate and exhaustive records of copulations during any given oestrous cycle, including number, sequence and proximity to ovulation, and larger sample sizes than are currently available for non-human primates. Experimental designs are difficult to implement with primates, and *in vitro* studies may constitute more a realistic approach to this question.

Technical challenges and outstanding questions

Overcoming technical challenges

Genotyping is a prerequisite for an understanding of the role of the MHC in mate choice, but can be surprisingly challenging in non-model organisms (taxa other than rodents and humans)[80]. For example, frequent duplications mean that genes are often found in multiple, tightly linked copies, so that single-locus amplification is impossible[80]. Separating sequences after multiple-locus amplification can be costly and time-consuming and usually requires high-quality DNA extracted from blood or tissue[81]. Invasive sampling of large numbers of study subjects raises logistic and ethical problems. Expression studies are also required to distinguish pseudogenes from functional genes[82] (only one existing study of non-human primates included expression analyses for some sequences[83]; others assumed that the MHC sequences produce functional molecules for pathogen resistance). The next generation sequencing technologies will help to overcome these difficulties, allowing large-scale genotyping[80]. Advances in non-human primate genomics will allow us to design new genotyping tools that span larger MHC regions, and may even allow the identification of microsatellite polymorphisms across the MHC region which will facilitate MHC typing[84] from non-invasive samples and allow us to identify exactly which genes are important in mate choice.

An outstanding question: the fitness consequences of mate choice

MHC-associated mate choice has long been thought to provide an ideal empirical opportunity to test theories of mate choice for indirect benefits[10,85]. However, few studies (and none in primates) have investigated whether such mate choice actually affects offspring fitness, although indirect evidence that it does comes from correlations between MHC constitution and resistance to particular pathogens[86-88]. Such findings may explain

choice for particular MHC genotypes, although as yet there is no choice documented for genotypes identified as conferring disease resistance. In addition, while disassortative mate choice has been commonly reported, the hypothesised advantage of MHC diversity for disease resistance has received mixed empirical support, although it may be apparent in the context of multiple infections[89,90]. Finally, particular host/pathogen interactions may not translate into MHC-associated fitness effects over a host´s lifetime. Future studies should concentrate on estimating the benefits of MHC-associated mate choice more directly, and clarifying the proximate pathways mediating such fitness effects, preferably in the same study population. The long lifespan of most primates complicates estimations of individual fitness, but primatologists have generated some of the longest-running field studies, making such investigations realistic. In the meantime, we expect the rapidly growing field of primate parasite ecology to create promising opportunities in this area[91].

The next-generation studies: within and across populations

As sample sizes and the prevalence of genetic paternity determination increase over time, we will become able to examine the consistency of mating decisions across females, compare genetic similarity in parents with that of random male-female dyads, examine offspring heterozygosity, and link the prevalence of extra-pair offspring to pair genetic similarity in pair-living species. We will be able to examine the consistency of patterns across consecutive generations, and explore how primates prioritise mate choice rules (for instance by favouring advantageous MHC genotypes over dissimilarity[92]), and integrate information perceived through multiple phenotypic cues[93]. Large-scale studies will allow us to examine inter-individual variation in MHC-dependent mating decisions in relation to the many factors that influence MHC-dependent mate choice (e.g., reproductive state and ethnic origin in humans[15]) and mate choice more generally[21]. Finally, detailed longitudinal studies will illuminate within-individual variation in mating decisions, and determine its mediators, such as fluctuations in the social[15] (e.g., involvement in long or short-term relationships for humans) or demographic context[94] (e.g., the pool of available partners).

At a larger scale, cross-population and cross-species variation in the form of MHC-biased mate choice expressed raises the question of which extrinsic factors modulate behavioural phenotypes. Addressing this requires studies across populations, harmonisation of data collection protocols and data-sharing. The wealth of information available regarding reproductive patterns across the primate order[21] will prove invaluable here. For instance, comparative studies of species or populations living in different environments or with different socio-sexual systems will allow us to examine whether factors linked to higher rates of parasite infection (such as larger group sizes or wetter environments[91]) influence MHC-dependent mating or post-mating behaviour. Likewise, cross-population comparisons will allow us to measure the influence of effective population size and genetic structure on MHC-dependent reproductive strategies, and reciprocally, the possible importance of MHC-biased reproductive strategies for the maintenance of genetic variation in isolated populations. For example, the loss of functional genetic diversity in response to habitat fragmentation may increase vulnerability to diseases in endangered species[95].

Finally, progress in evolutionary studies of the MHC is conditional on progress in numerous adjacent fields, including immunogenetics, genomics, immunology, parasitology, virology, bacteriology, reproductive physiology, cellular biology and biochemistry so future studies should be prepared to take a truly transdisciplinary angle.

CONCLUSION

Two key points make primates interesting in the context of MHC-associated mate choice: the fact that humans are primates, and the diversity of primate mating and social systems. As a result, the primate order offers the possibility of combining (1) studies of mate choice and fitness consequences (in non-human primates), with (2) in depth characterisation of mate preferences through experimental settings (humans). This methodological complementarity provides an exceptional opportunity to achieve a better understanding of the role of MHC in mate choice in human and animal societies. The handful of existing studies shows that primates exhibit all three forms of MHC-associated mate choice: choice

for a good combination of genes in the offspring, choice for an MHC-diverse mate, and choice for particular MHC genotypes, suggesting that mate choice for genetic quality can coexist with constraining social rules. A major task for the future is to understand the mechanisms and priority rules, if any, that structure and order these seemingly complex processes, including weighting the influence of MHC in relation to the many other possible criteria for mate choice, and the influence of a given form of MHC-biased mate choice in relation to others. The proximate mechanisms underlying MHC-associated choice are as yet barely examined, but experiments on human mate preferences and new perspectives in the study of primate signalling pave the way for a new understanding of pre-copulatory choice. In contrast, logistical challenges associated with the study of post-copulatory processes obscure their potential importance in primates. The resolution of technical difficulties in data production and analysis should encourage researchers to address outstanding theoretical questions which will shed important light on the evolution of human and non-human behaviour. These include tests of the actual fitness consequences of mate choice strategies within populations and characterizing the social and environmental influences that mediate the role of MHC in sexual behaviour within individuals and populations, as well as across populations.

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Figure 1. The five species of non-human primate in which MHC-associated mate choice has been studied. Clock-wise from left: fat-tailed dwarf lemur (photo by Manfred Eberle); chacma baboons at Tsaobis, Namibia (photo by Elise Huchard); rhesus macaques on Cayo Santiago (photo by Lauren Brent); grey mouse lemurs (photo by Manfred Eberle); mandrills at CIRMF, Gabon (photo by Jo Setchell). The lack of an image of dwarf lemurs copulating illustrates the difficulty of studying primate sex in the wild.

Figure 2. Primate ornaments that signal the possession of specific MHC class II supertypes. Left: the red facial coloration of a male mandrill at CIRMF (photo by Jo Setchell); Right: the size and morphology of chacma baboon sexual swellings (photo by Elise Huchard).

Table 1. Summary of studies of MHC-associated mate choice in non-human primates

Species and source	Social and mating system	Population type	Loci studied[a]	Design and sample size	Choice for MHC dissimilarity	Choice for MHC diversity	Choice for intermediate MHC diversity	Choice for specific MHC genotypes
Rhesus macaque (*Macaca mulatta*) ; ref [96]	Multi-male, multi-female; female philopatry; polygynandrous	Large, genetically isolated semi-free ranging population	MHC class II DQB1	Mating outcomes (541 pairs) and RS (120 males)	No	Yes (males)	NA	NA
Grey mouse lemur (*Microcebus murinus*) ; ref [97]	Solitary foraging; female philopatry; polygynandrous	Wild	1-2 MHC class II DRB loci (sequences , supertypes , aa differences); 17 microsatellites	Behavioural mate choice (21 females); mating outcomes (79 offspring)	Yes (but only for mating outcomes, using supertypes and aa)	Yes (but only for mating outcomes, using supertypes and aa)	NA	No
Fat-tailed dwarf lemur (*Cheirogaleus medius*); ref [97]	Socially monogamous with high extra-pair paternity; female philopatry???	Wild	1-2 MHC class II DRB loci (sequences , supertypes , aa differences	Choice of social partner (21 pairs); mating outcomes (43 offspring including 17 extra-pair	Yes (for both social mate and sires, but using supertypes only)	Yes (for both social mate and sires, but using sequences and supertypes only)	NA	Yes (for social mate only)

			); 7 microsatellites	offspring)				
Mandrill (*Mandrillus sphinx*) ; ref [83]	Multi-male, multi-female; female philopatry; polygynandrous	Large, genetically isolated semi-free ranging population	1-4 MHC class II DRB loci (sequences, supertypes, aa differences, Expression analyses); 8-10 microsatellites	Mating outcomes (180 offspring); RS of 40 males	Yes	Yes	No	No
Baboon (*Papio ursinus*) ; ref [30]	Multi-male, multi-female; female philopatry; polygynandrous	Wild	1-4MHC class II DRB loci (sequences, supertypes, haplotypes); 16 microsatellites	Mating outcomes (59 offspring); RS (64 females); comparison of genetic population structure for MHC and microsatellites (6 groups, 199 individuals)	No	No	No	No (examined choice for rare, not specific genotypes)

RS = reproductive success; aa = amino acid