The Royal Society

MHC-disassortative mating preferences reversed by cross-fostering

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House mice (*Mus musculus domesticus*) avoid mating with individuals that are genetically similar at the major histocompatibility complex (MHC). Mice are able recognize MHC-similar individuals through specific odour cues. However, to mate disassortatively for MHC genes, individuals must have a referent, either themselves (self-inspection) or close kin (familial imprinting), with which to compare the MHC identity of potential mates. Although studies on MHC-dependent mating preferences often assume that individuals use self-inspection, laboratory experiments with male mice indicate that they use familial imprinting, i.e. males learn the MHC identity of their family and then avoid mating with females carrying 'familial' MHC alleles. To determine if female mice use familial imprinting, we cross-fostered wild-derived female mouse pups into MHC-dissimilar families, and then tested if this procedure reversed their mating preferences compared with in-fostered controls. Our observations of the female's mating behaviour in seminatural social conditions and the genetic typing of their progeny both indicated that females avoided mating with males carrying MHC genes of their foster family, supporting the familial imprinting hypothesis. We show that MHC-dependent familial imprinting potentially provides a more effective mechanism for avoiding kin matings and reducing inbreeding than self-inspection.

Keywords: major histocompatibility complex; sexual selection; chemosensory imprinting; kin recognition; inbreeding avoidance

1. INTRODUCTION

The genes of the major histocompatibility complex (MHC) are the most polymorphic coding loci known among vertebrates, and their products, MHC molecules, play a central role in immunological self/non-self recognition (Klein 1986; Janeway 1997). House mice (*Mus musculus domesticus*) prefer to mate with individuals carrying dissimilar MHC genes under laboratory (Yamazaki *et al*. 1976; Egid & Brown 1989) and seminatural conditions (Potts *et al*. 1991). Humans prefer the odour of MHC-dissimilar individuals (Wedekind *et al*. 1995; Wedekind & Füri 1997) and there is evidence that humans have MHC-disassortative mating preferences (Ober *et al*. 1997). MHC-dependent mating preference may function to produce disease-resistant, MHC-heterozygous offspring, to reduce inbreeding, or both (Potts & Wakeland 1993; Brown & Eklund 1994; Apanius *et al*. 1997). House mice can discriminate the odours of individuals that differ genetically only at a single MHC locus, which indicates that MHC genes influence individual odours (Yamazaki *et al*. 1979; Penn & Potts 1998*b*; reviewed in Penn & Potts (1998*a*)). To mate disassortatively for MHC genes, individuals must have a referent with which to compare potential mates (Lacy & Sherman 1983). It is often assumed that individuals inspect themselves and then avoid mating with others expressing similar MHC genes (self-inspection or the 'armpit effect') (e.g. Wedekind *et al*. 1995; Hedrick & Black 1997). Yet another possibility is that individuals learn the MHC-determined odours of their close kin in their natal nest and then avoid mating with individuals carrying 'familial' MHC genes (negative familial imprinting).

Laboratory experiments with male house mice suggest that MHC-dependent mating preferences are controlled by familial imprinting. An initial serendipitous observation suggested that mating preferences of male mice were dependent upon the MHC genotype of his parents and his exposure to the odours of other mouse strains (reviewed in Beauchamp *et al*. (1988)). To test this hypothesis, Yamazaki *et al*. (1988) experimentally fostered male mice at birth with MHC-dissimilar (cross-fostered) or MHC-similar (in-fostered) parents and tested their mating preferences at sexual maturity. Cross-fostered males preferred to mate with MHC-similar females, avoiding MHC-dissimilar females that carried the MHC haplotypes of the male's foster parents. This experiment was successfully repeated with a second strain of male MHC-congenic mice; however, no preferences were found with the cross- or in-fostered females (Beauchamp *et al*. 1988). A recent laboratory study with female mice found some evidence that cross-fostering altered the mating preferences of one of two strains of female mice (Eklund 1997).

There are several reasons why the evidence from these laboratory studies with mice should be treated with caution (Manning *et al*. 1992*a*; Penn & Potts 1998*a*). First,

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Received 23 February 1998 *Accepted* 23 March 1998

the previous laboratory studies have relied on rather indirect evidence for mating preferences, such as the presence of copulatory plugs and first-mount preferences. For example, the 'mating preferences' of female mice reported by Eklund (1997) were only first-mount preferences; there were no ejaculatory preferences. Yet, mounts and intromissions, which precede ejaculation (non-ejaculatory copulations), may not reflect mating preferences, as rodents appear to use non-ejaculatory copulations as courtship assessment (Dewsbury 1988). Second, laboratory conditions can create artefacts due to artificial social conditions, tethering animals, inducing oestrus in females and vasectomizing males. Third, the disparate results obtained among strains of mice may simply be an artefact of inbreeding during strain derivation, thus making it impossible to draw strong conclusions about wild mice (Manning *et al*. 1992*a*). Fourth, the only evidence for MHC-dependent familial imprinting in female mice failed to use in-fostered mice to control the possibility that alterations in mating preferences were an artefact of the fostering procedure (Eklund 1997). It is important to determine if female mice use familial imprinting because females do not necessarily use an imprinting mechanism and selection on MHC genes from mating preferences appears to be driven mainly by females rather than males (Egid & Brown 1989; Eklund *et al*. 1991; Potts *et al*. 1991).

To determine if female house mice use familial imprinting, we cross-fostered wild-derived female mice and released them into large, seminatural enclosures containing MHC-similar and MHC-dissimilar males. We used the genotypes of the female's offspring as well as observations of their mating behaviour to determine a female's mating preferences. If cross-fostered females avoid mating with MHC-similar males, then this would indicate that females use self-inspection. However, if cross-fostered females prefer MHC-similar males to MHC-dissimilar males who are identical to the female's foster family, then this would indicate that females use familial imprinting.

2. METHODS

The animals in this experiment were derived from wild-caught house mice that were crossed with inbred strains carrying known MHC haplotypes (Potts *et al*. 1991). Among the F2 generation, only the MHC homozygotes carrying the known haplotypes were used to continue the outbred colony. This breeding scheme was designed to create mice that were genetically semi-wild, and yet carried well-characterized MHC haplotypes. We used mice that were homozygous for two MHC haplotypes, *k* and *q*, derived from the B10.BR and DBA/1 strains, respectively. The mice were housed under standard conditions ($22 \pm 2\,^{\circ}$C, 12:12 h light:dark cycle, light on at 08.00) in 13 cm × 18 cm × 29 cm acrylic mouse cages. Food and water were available *ad libitum*. The two strains were housed in separate rooms to prevent odour mixing. We conducted this experiment from September 1995 to October 1996, at the University of Florida, Gainesville, Florida, USA.

We bred 40 pairs of the semi-wild mice to produce MHC-homozygous offspring (*kk* and *qq*). We checked breeding cages every day for pregnant females and litters. Within 24 h after birth, we sexed all of the pups (using anogenital distance), and then fostered a single female pup from each litter into an MHC-dissimilar (cross-foster) or MHC-identical (in-foster) family. A family included a nursing dame, a sire and their pups. To distinguish the fostered pup from their foster siblings, we docked the tail tips of each fostered pup while they were under anaesthesia (Metophane). Nineteen of the 134 fostered pups died before weaning; mortality did not differ between the cross-fostered and in-fostered pups ($\chi^2 = 0.1$, $n = 134$, $p > 0.25$). We weaned the fostered female mice at 21 days, hole-punched their ears (while under anaesthesia) for identification, and then housed each female separately.

After the fostered females reached sexual maturity (3 months of age in the first group of replicates and 6 months in the second), we released them into one of four large (49 m^2) population enclosures. Each enclosure was subdivided into eight equal subsections by 46 cm high hardware cloth (1.25 cm grids). The mice could climb over this screening within the enclosures; the dividers provided environmental heterogeneity and barriers which males tend to use for territorial boundaries. Each subsection contained food, water, bedding material, nest boxes and an additional spiral of hardware cloth. Each population was founded by 12 females, identical for their MHC genotype (*kk* or *qq*) and fostering treatment (cross- or in-fostered), and six males, three MHC-similar and three MHC-dissimilar to the females. For the cross-fostered females, the dissimilar males were MHC-identical to the female's foster family. The males were age-matched and unrelated to each other and the females. For each of the four populations of cross-fostered females that we tested, we simultaneously tested the preferences of an in-fostered population of females in an adjacent enclosure as a control. The first four populations were run for 14 weeks, from February to June 1996, and the second four also ran for 14 weeks, from June to September 1996.

We conducted behavioural observations 5–7 days per week for 1–4 h per day. We observed the mice at dusk, when they are most active, under dim red light using flashlights and close-focus binoculars to identify individuals by their unique ear punches. Observers were unaware of the MHC genotypes of the mice and recorded sexual interactions from outside the enclosures using *ad libitum* sampling. We defined a 'mating bout' as a male performing one or more mounts, intromissions or ejaculations with a particular female. Males perform up to 50 intromissions with the same female during mating (Estep *et al*. 1975), but we considered such a series as a single mating bout. Multiple mating bouts between the same individuals on different nights were excluded from the analyses because of the potential lack of independence. We also analysed the number of mount and intromission bouts. However, rather than giving equal weight to mounts, intromissions and ejaculations, we calculated an overall 'mating score' for MHC-similar versus MHC-dissimilar males by weighting these three mating behaviours: $\Sigma[\Sigma(\text{mount bouts} \times 0.1) + \Sigma(\text{intromission bouts} \times 0.3) + \Sigma(\text{ejaculations} \times 0.6)]$. The relative weightings were decided before inspecting the data.

Previous observations indicate that subordinate males are less likely to mate than dominant males, which suggests that random mating expectations should be adjusted to reflect any differences in dominance status among males (Potts *et al*. 1991). Therefore, we collected data on dominance interactions among the males, including tail rattle displays, agonistic chases and fights. 'Dominant males' were defined as the males that performed the majority of these agonistic behaviours. Because subordinate males sometimes achieve copulations (D. Penn & W. Potts,

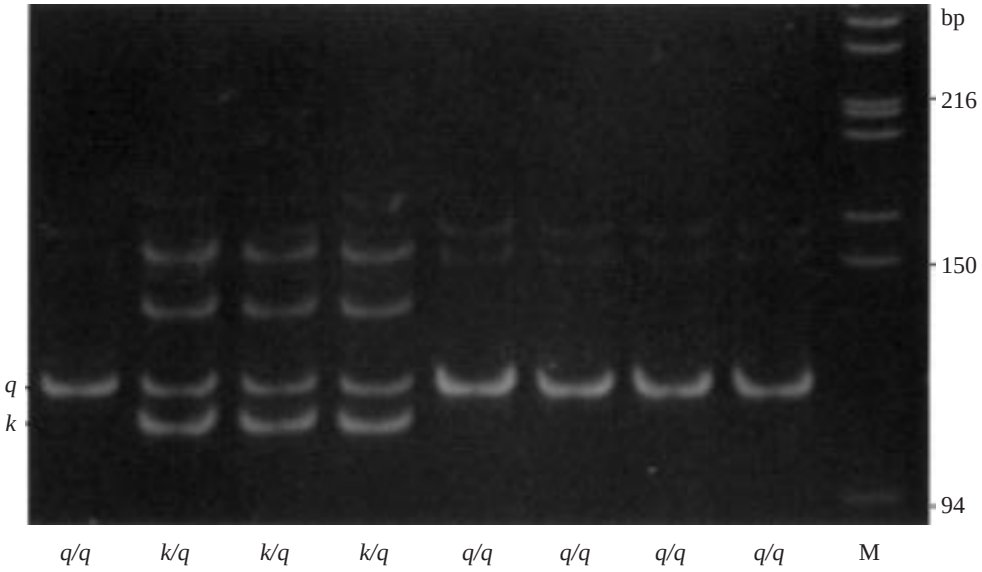

Figure 1. Ethidium-bromide-stained polyacrylamide gel showing the PCR amplification products of an MHC-linked microsatellite locus that discriminates the *k* and *q* haplotypes. Each lane shows the MHC genotype of an individual progeny, which enabled us to determine if it was sired by an MHC-similar or MHC-dissimilar mating. M = λPst marker.

Table 1. *The total number of matings observed with males of different MHC classes among females with different foster treatments*

(The number of ejaculations performed with MHC-similar versus MHC-dissimilar males was dependent upon a female's fostering treatment (Fisher's Exact test, $p=0.03$, $n=22$). The three types of mating behaviours that we recorded were combined into a single, weighted 'mating score' (see §2), which also differed significantly between cross-fostered and in-fostered females ($\chi^2 = 6.3$, d.f. = 1, $p<0.025$).

female's fostering treatment	total mating bouts			
	mounts	intromissions	ejaculations	mating score
cross-fostered				
MHC-similar	34 (85%)	11 (65%)	9 (81%)	12.1
MHC-dissimilar	6 (15%)	6 (35%)	2 (9%)	3.6
in-fostered				
MHC-similar	13 (54%)	17 (53%)	3 (27%)	8.2
MHC-dissimilar	11 (46%)	15 (47%)	8 (73%)	10.4

personal observations), we analysed the data using all males, as well as using the expectations adjusted for dominance, which we report when the two results differed. This approach also allowed us to eliminate the possibility that any apparent non-random mating preferences were due to increased dominance of MHC-similar or MHC-dissimilar males.

As we observed only a fraction of the matings that occurred in the eight populations over the seven months, we also determined the MHC genotype of the progeny that were born in the enclosures to evaluate the MHC mating patterns of the mice. We collected all of the pups that we found on daily nest checks, killed them with an overdose of anaesthesia (Metophane), and then collected a tissue sample that was frozen at −20 °C. The tissue samples were digested using lysis buffer and proteinase K and the DNA was extracted using ammonium acetate. The progeny were genotyped using a microsatellite marker closely linked to the MHC (Saha & Cullen 1986). Allelic polymerase chain reaction (PCR) amplification products were resolved using ethidium-bromide-stained polyacrylamide gels (Potts 1996) (figure 1). There were only two possible MHC genotypes of progeny, MHC homozygotes or heterozygotes, which were the result of MHC-assortative or MHC-disassortative matings, respectively. To assess mating preferences, we compared the number of pups from MHC-assortative versus MHC-disassortative matings in the cross-fostered populations with those from the in-fostered control populations (using contingency χ^2 tests). We also analysed the standardized residuals in these comparisons to determine which of the deviations from expected created the significant effects (Siegel & Castellan 1988).

3. RESULTS

Our behavioural observations indicated that females in the cross-fostered populations were more likely to mate with MHC-similar males, whereas females in the in-fostered populations tended to mate with MHC-dissimilar males (table 1). Among the cross-fostered females, we observed 11 ejaculations, nine of which were with MHC-similar males (Binomial test, $p=0.03$). This pattern was significantly different from the in-fostered females, in which eight of the 11 ejaculations observed were with MHC-dissimilar males (Fisher's Exact test, $p=0.03$, $n=22$). The mating scores, which also took

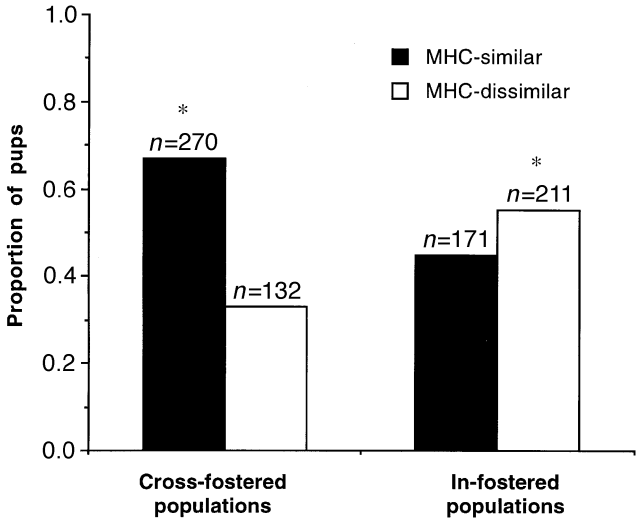

Figure 2. The proportion of pups from MHC-similar and MHC-dissimilar matings compared between cross-fostered and in-fostered female mice ($\chi^2 = 39.9$, $n=784$, $p<0.0001$). The type of mating was deduced from pup MHC genotypes (see § 2). The values above the bars refer to the number of pups in each category (* indicates that the standardized residuals were positive and significant at $p=0.05$).

mounting and intromission bouts into account, showed the same pattern. Among the cross-fostered females, the mating score was higher for MHC-similar than for MHC-dissimilar matings, whereas among the in-fostered females, the mating score was significantly higher for MHC-dissimilar matings ($\chi^2 = 6.3$, d.f.$=1$, $p<0.025$).

The MHC genotypes of the progeny also indicated that cross-fostered females were more likely to mate with MHC-similar males, whereas in-fostered females were more likely to mate with MHC-dissimilar males (figure 2). Among the offspring of the cross-fostered females, 67% of the pups were from matings with MHC-similar males. This pattern was reversed from the in-fostered females, in which only 45% of the offspring were sired by MHC-similar males ($\chi^2 = 39.9$, $n=784$, $p<0.001$). Although the mating preferences of the cross-fostered mice appear to be greater than the in-fostered mice, this difference is not statistically significant ($\chi^2 = 0.006$, $n=784$, $p>0.9$). Assortative mating preferences of cross-fostered populations could not be attributed to an incidental increase in dominance success of MHC-similar males since, overall, approximately half (48%) of the dominant males were MHC-similar to the females. Similarly, the disassortative patterns among the in-fostered populations were unlikely to be due to an increase in dominance success of MHC-dissimilar males because half (50%) of the dominant males were MHC-dissimilar to the females.

When the genotypes of progeny are compared among the four replicate groups, the first two replicates show a consistent pattern, i.e. most of the pups were sired by matings with MHC-similar males in the two cross-fostered populations, whereas the two in-fostered populations show the reverse pattern. In the first population of cross-fostered *qq* females, 84% of offspring were from MHC-assortative matings. In contrast only 41% of the offspring were from MHC-assortative matings in the first in-fostered *qq* population ($\chi^2 = 30.7$, $n=180$, $p<0.0001$) (figure 3*a*). Similarly, in the first population of cross-fostered *kk* females, 77% of offspring were from MHC-assortative matings, whereas 31% of the offspring were from MHC-assortative matings in the first in-fostered *kk* population ($\chi^2 = 41.9$, $n=202$, $p<0.0001$) (figure 3*b*). The MHC-genotypes of the progeny from the second two replicates did not show such a consistent pattern. In the second cross-fostered population of *qq* females, 66% of the pups were from MHC-assortative matings, which differed significantly from the in-fostered controls ($\chi^2 = 7.0$, $n=243$, $p<0.01$), but the in-fostered controls appeared to mate randomly (figure 3*c*). The second populations of *kk* females were anomalous relative to the first three replicates: the mating patterns of the cross-fostered females were consistent with random mating expectations, and the progeny from the in-fostered females were consistent with an MHC-assortative mating preference (figure 3*d*) ($\chi^2 = 5.2$, $n=163$, $p<0.05$).

The one cross-fostered population that did not show an assortative pattern (the second *kk* population; figure 3*d*) can be explained by an increased survival and dominance of the MHC-dissimilar males in this population. One of the three MHC-similar males in this population died during the experiment, and once the expected MHC genotypes of the pups were calculated from the surviving males, the offspring were significantly more likely to be fathered by MHC-similar males ($\chi^2 = 7.3$, $p<0.005$). In addition, when the expected MHC genotypes were calculated using the dominant males, the assortative pattern is even more significant ($\chi^2 = 17$, $p<0.0001$). Thus, there were actually fewer pups from matings with MHC-familial males in the fourth population of cross-fostered females when differential survival and dominance of the males in this population are taken into account.

4. DISCUSSION

The results from both observations of mating behaviour and MHC genotyping support the familial imprinting hypothesis, i.e. that female mice learn the MHC identity of their parents and then avoid mating with individuals carrying familial MHC genes. Our observations of mating behaviour indicated that cross-fostered females preferred to mate with MHC-similar males over males that were MHC-dissimilar but identical to their foster families (MHC-familial). This pattern was consistent whether we used only the number of ejaculations or an overall mating score that also considered the number of mounts and intromission bouts observed. The genetic parentage of the progeny of the cross-fostered females also indicated that females avoided mating with males carrying familial MHC genes. Among the four populations of cross-fostered females, only 33% of the progeny were from matings with MHC-dissimilar (familial) males. This result is strikingly different from the MHC-disassortative mating pattern observed in unfostered populations of wild-derived mice living in similar conditions (Potts *et al.* 1991). The avoidance of MHC-familial males by cross-fostered females was not an artefact of the fostering procedure because the in-fostered females, like unfostered females, tended to mate with

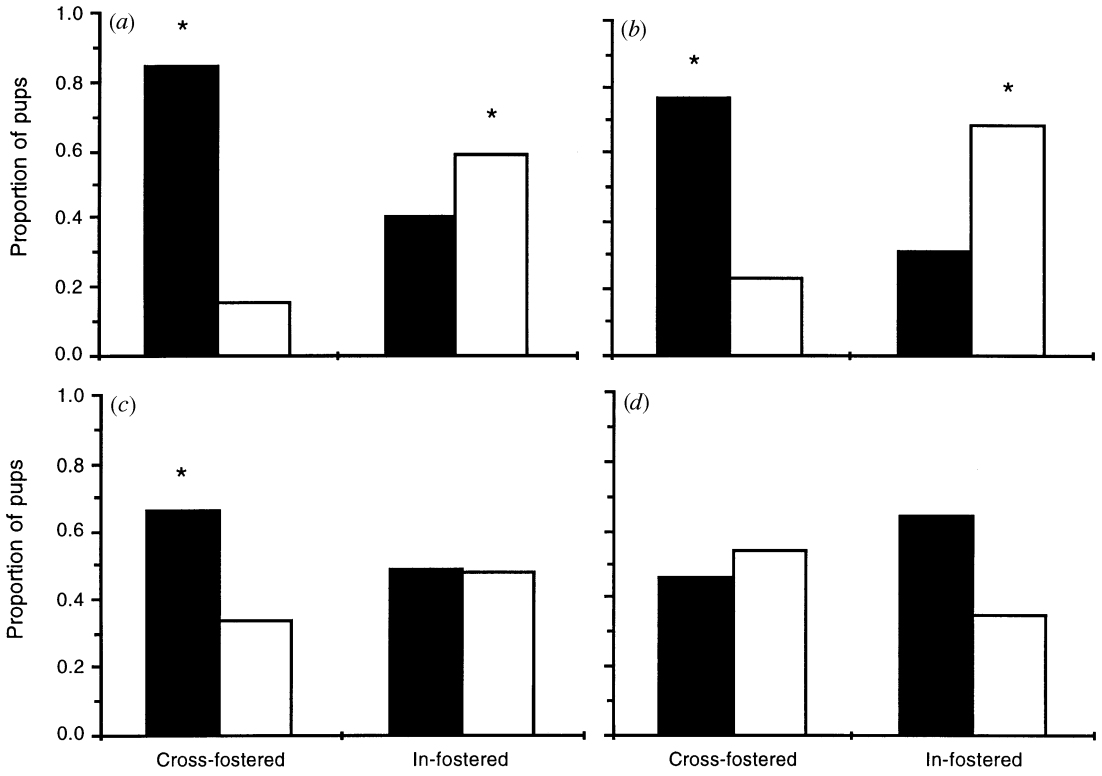

Figure 3. The proportion of pups from MHC-similar (filled bars) and MHC-dissimilar (empty bars) matings in the four replicate groups. (*a*) The first population of cross-fostered *qq* females versus the in-fostered *qq* population ($\chi^2 = 30.7$, $n=180$, $p<0.0001$). (*b*) The first population of cross-fostered *kk* females versus the in-fostered *kk* population ($\chi^2 = 41.9$, $n=202$, $p<0.0001$). (*c*) The second population of cross-fostered *qq* females versus the in-fostered *qq* population ($\chi^2 = 7.0$, $n=243$, $p<0.01$). (*d*) The second population of cross-fostered *kk* females versus the in-fostered *kk* population ($\chi^2 = 5.2$, $n=163$, $p<0.05$). (* indicates that the standardized residuals were positive and significant at $p=0.05$).

MHC-dissimilar males and 55% of the progeny were sired by matings with MHC-dissimilar males.

When we analysed the progeny genotypes from each population separately we found some variation among populations. One of the in-fostered control populations showed no difference (figure 3*c*) and another showed an anomalous pattern (figure 3*d*). The second population of in-fostered *qq* females had roughly equal number of pups from MHC-similar and MHC-dissimilar matings, suggesting no mating preferences (figure 3*c*). There was a flood in this population which caused the death of one of the two dominant *kk* males and two litters of pups in his territory. After the death of this male, three of the other males fought violently for several weeks over his territory. Perhaps females under stressful conditions do not have the luxury of being choosy about their mate's MHC genotype. The second population of in-fostered *kk* females (figure 3*d*) had more pups from MHC-assortative matings. This anomalous pattern could not be explained by a bias in the death or dominance of MHC-similar males. It is unclear why the results of the second group of replicates was not as robust or consistent as the first. The females in the second group of replicates were in captivity longer and were three months older than the first females, so perhaps increased age or time in captivity makes females less choosy. The variation in behaviour among individuals is understandable when one remembers that mating preferences in mice are based on many characters, not just MHC identity, which vary among individuals in seminatural conditions.

There is always a potential problem with naturalistic studies because individuals may not behave independently (Martin & Bateson 1993). One potential independence problem is that females may copy each other's behaviour. Although this possibility cannot be excluded in our experiment, our observations in this and previous studies do not suggest that females copy each other's mating preferences (Potts *et al.* 1991). Independence assumptions would also be violated if house mice were monogamous, so that once a male mated he would no longer be available. However, male house mice are polygynous and females mate multiply (Potts *et al.* 1991). Indeed, multiple paternity is the reason that we could not treat each litter as an independent unit. Treating pups as independent units may not be unrealistic, as pregnant females may use mechanisms to preferentially select the sperm or foetuses of MHC-dissimilar mates (Wedekind 1994). Thus, it is difficult to see how a lack of independence among individuals could explain these results.

Although this study provides further evidence for MHC-dependent mating preferences in wild-derived female mice in seminatural conditions (Potts *et al.* 1991), it does not exclude the possibility that males also have mating preferences. MHC-dependent mating preferences have been found in male mice under laboratory conditions (Yamazaki *et al.* 1976, 1988; Beauchamp *et al.*

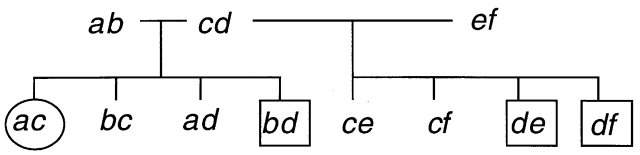

Figure 4. Examining the MHC genotypes of closely related mice reveals that self-inspection would not provide a particularly effective mechanism for avoiding kin matings (this pedigree is typical for house mice in the wild, as most individuals are heterozygous at MHC loci because these genes are highly polymorphic). For example, if female *ac* uses self-inspection, then she will risk mating with one-fourth of her siblings (*bd*) and one-half of her half-siblings (*de* and *df*). Familial imprinting, in contrast, would provide a more effective inbreeding avoidance mechanism. If female *ac* uses familial imprinting, then she can effectively avoid mating with her kin, including all full siblings (*ab*, *bc*, *ad*, *bd*), all half-siblings (*ce*, *cf*, *de*, *df*), and half of all cousins. As house mice are often reared in communal nests and nursed by their aunts (Wilkinson & Baker 1988; Manning *et al*. 1992*b*, 1995), familial imprinting may enable females to avoid mating with all close cousins.

1988), although it is unclear if males express preferences in natural conditions. There are reasons to suspect that male mice may be choosy (Dewsbury 1982), but theoretical work and empirical observations suggest that males are not as choosy as females (e.g. mate choice studies sometimes have a difficult time detecting even a species preference in males) (D'Udine & Alleva 1983). The males in our experiment did not have an opportunity to be choosy with respect to a female's MHC, as all of the females within each population had the same MHC genotype.

Many studies have found that rodents imprint on familial odours during early ontogeny and this experience alters their sexual preferences as adults (Leon 1983; D'Udine & Alleva 1983; Fillion & Blass 1986). Although it is not known precisely how chemosensory imprinting occurs, many studies have found that exposure to odours during early ontogeny alters the development of the main olfactory bulb (Harvey & Cowley 1984; Woo *et al*. 1987; Sullivan *et al*. 1989; Wang *et al*. 1993), the neural centre that processes information sent by olfactory receptors and relays it to the olfactory cortex and other regions of the brain (Buck 1996). It is unclear from this study and others, however, if chemosensory imprinting has a critical period (i.e. 'imprinting' in the classical sense). Interestingly, it appears that rodent pups do not imprint indiscriminately on odours to which they are exposed in the nest, but rather they imprint on specific olfactory cues associated with particular stimuli, such as maternal grooming (directed learning) (Leon *et al*. 1987; Terry & Johanson 1996).

Why do mice negatively imprint on MHC-determined odours and avoid mating with individuals carrying familial MHC genes? If MHC-dependent mating preferences function to produce MHC-heterozygous offspring, then females should simply avoid mating with MHC-similar males (self-inspection); familial imprinting would only increase the avoidance of suitable mates. If MHC-dependent mating preferences function to reduce inbreeding (Potts & Wakeland 1993; Potts *et al*. 1994), then familial imprinting may provide a more effective mechanism to avoid kin matings than self-inspection alone (figure 4). Learning genetically determined odour cues of family members would help to explain how house mice are able to recognize kinship among unfamiliar individuals (Winn & Vestal 1986; König 1994). However, familial imprinting will be an error-prone mechanism if extra-pair matings are common and individuals imprint indiscriminately on nest mates. Yamazaki *et al*. (1988) cross-fostered entire litters, which suggests that males do not use siblings as referents. MHC-dependent maternal imprinting by itself would still allow individuals to avoid mating with three-quarters of their siblings and one-half of their half-siblings. Mice may use other loci, besides the MHC, and they may also use self-inspection as well as familial imprinting to recognize unfamiliar kin. The results of this study do not exclude these other possibilities, but they are consistent with the hypothesis that the MHC provides a kin recognition cue to reduce inbreeding (Potts & Wakeland 1993; Brown & Eklund 1994).

5. CONCLUSIONS

The results of our study have several implications for understanding the underlying mechanisms and functions of MHC-dependent mating preferences.

1. This study provides experimental support for the original discovery of MHC-dependent mating preferences in seminatural populations of house mice (Potts *et al*. 1991).
2. It also provides further evidence for MHC-dependent mating preferences in female mice (Egid & Brown 1989; Potts *et al*. 1991).
3. This study shows that female mice avoid mating with males carrying familial MHC genes, and provides the first evidence that MHC-dependent imprinting alters the mating preferences of mice living in seminatural conditions.
4. This study is consistent with the hypothesis that MHC-dependent mating preferences function to reduce inbreeding and suggests that familial imprinting provides a more effective mechanism for reducing inbreeding than self-inspection.
5. This study has relevance for odour-mediated mating preferences (Herz & Cahill 1997) and kin recognition in humans (Porter & Moore 1981). It has long been known that childhood familiarity abolishes sexual interest among adults and that this individual imprinting mechanism functions to reduce inbreeding (the Westermarck hypothesis) (for a review, see Wolf (1995)). A recent study now suggests that people also avoid mating with individuals if they carry MHC genes similar to their mother's MHC (Ober *et al*. 1997).

We thank our assistants who provided much help in this project, especially B. Aguyo, D. Andersen, A. Bogle, M. Ellsworth, K. Hansen, R. Ketola, S. Keovilay, R. Long, K. Marchant, L. Morrison, B. Nelson, J. Sanchez and L. Taylor. We thank Dr Jane Brockmann, Dr Jo Manning, Dr Carla Restrepo and Dr Claus Wedekind for their useful suggestions. We also thank the Department of Zoology at the University of Florida and the Department of Biology at the University of Utah. This research

was funded by a grant to W.P. from the National Science Foundation (IBN 9222177).

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