Of mice and the MHC

Alan Grafen

Do mice recognize their kin? They are known to discriminate between conspecifics through the products encoded by the highly polymorphic loci of the major histocompatibility complex (MHC)[1]; the MHC is not only involved in immune recognition, but also affects an individual's odour profile. There is, however, a general methodological reluctance to accept such discrimination as evidence of kin recognition[2]. It was shown last year[3] that female mice prefer mating with males that differ from them at the MHC locus and now, on page 581 of this issue[4], the same authors (C. J. Manning, E. K. Wakeland and W. K. Potts) show that females nest communally with other females that are similar at the MHC. Smelling MHC differences seems to be important in the social lives of mice.

The technique of Manning and colleagues is to put the geneticist's knowledge of inbred strains, breeding designs and MHC-typing to the service of behavioural ecology. Seminatural conditions allow freedom of mating and communal nesting, and individual tags mean that the mice can be observed without disruption.

Around the time a female mouse gives birth, she usually finds a nestmate who has just given birth. The two females (sometimes more) suckle the pups indiscriminately. Manning *et al.* compared the nestmate that was chosen by each female with the other females that could have been chosen instead. They found that the MHC similarity was significantly greater with the chosen nestmate. The genetic manipulations allowed relatedness and MHC similarity to be uncorrelated in some of the groups, so the preference for MHC could not be explained by females choosing relatives according to a general background of genetic similarity. The MHC locus stood out as the focus of choice. These results should encourage workers on kin recognition in other species to investigate the importance of genetic discrimination in natural conditions.

We have one well-documented example of kin recognition in the ascidian *Botryllus schlosseri*, larvae of which tend to settle with histocompatible individuals[5]. Can mice be taken as a second example? Certainly Manning *et al.* have shown that the discrimination is used in nature, and this in itself is very important. It is still worth asking whether it counts as kin recognition, the essential question being whether mice choose nestmates according to MHC alleles in order to help relatives.

Manning *et al.* refer to "expectations that kin will be preferred as nesting partners". In a recent theoretical study[6], Giraldeau and Caraco have tackled the issue of whether kin selection should lead to kin groups, and the answer is subtle. There is no general presumption. Some concepts can be introduced with some starkly simplified examples based on the nesting of mice.

(1) Two sets of two sisters give birth on the same day, and nests are big enough for only two females. If success in rearing pups is unaffected by the relatedness of nestmates, then there is no kin-selective reason why the sisters should pair up.

C. J. Manning

Suckling cousins? A single female mouse nurses the broods of her nestmates.

(2) Suppose there are two sets of two sisters and one extra female. There is a disadvantage to nesting alone, and two sisters should pair up if this makes it less likely that either of them will end up as the odd one out.

(3) Suppose there are two sisterhoods of three and four. A quick-counting member of the three would try to pair up with one of the four. When the others realized what was happening, and paired up with sisters, it would be one of the original four that was the odd one out.

These examples are meant to show that any warm cosy feeling animals may gain from grouping with kin is not enough. A kin-selective advantage must come about through differential effects on number of offspring of the options of pairing with kin and not doing so. They are also meant to show that in some circumstances it may actually be advantageous to group with non-kin[6].

Returning to the real world, should mice really prefer to nest with kin? It does seem likely that, in general, nesting with kin would reduce the chance that kin end up nesting alone. To this extent it would be churlish to deny mice parity with *B. schlosseri*. But this tentative acceptance as kin recognition would be placed in doubt if it were shown that helping kin was not the major selective force. For instance, a possible reason for preferring similarity at the MHC locus is that females may discriminate between their own pups using the MHC. A female may prefer to belong to a nest in which both nestmates find it more difficult to distinguish their own pups, as this may increase effective cooperation. That would be an interesting selective force, but not a kin-selective one.

A point not explicitly made by the authors can be drawn tentatively from their Table 2 (see page 582). A female seems to match the MHC of potential nestmates against a referent that is derived from the haplotypes present in her own natal nest, and not from her own genotype. More direct evidence of this would be welcome. For one thing, the workings of the recognition system are of interest in themselves. Further, if females choose in an evolutionary sense to use a natal nest referent rather than their own MHC alleles, this may reflect on the selective forces involved. Specifically, is natal-nest MHC similarity really the best cue females have for kinship?

One technical reservation concerns the breeding scheme used to derive the experimental mice in which relatedness and MHC similarity were uncorrelated. Only a few generations elapsed between the founders and the experimental animals. So far as I can see, it follows that a large stretch of chromosome on either side of the MHC locus is likely to share similarity with the MHC locus. Not enough crossovers have had time to occur to restrict the conclusions definitively to that locus rather than one nearby, but this point does not threaten the rejection of general genetic similarity across all chromosomes as the effective variable.

Recognition systems are harder to study in nature than in the laboratory. But they are much more informative too. □

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