Does MHC Influence Human Mate Choice?

IHARA Yasuo

The University of Tokyo, Japan

Abstract

MHC (major histocompatibility complex), known in humans as HLA (human leukocyte antigen) and in mice as H-2, plays an important role in the immune system. The principal function of MHC molecules is to present antigens to T-cells to initiate an immune response against nonself. There are a large number of alleles at the MHC loci and this produces so many different combinations that virtually no two individuals are identical in their MHC genotype. The high degree of polymorphism is thought to be maintained by balancing selection such as overdominant or frequency-dependent selection from pathogens and/or mating preferences. House mice are more likely to mate with individuals dissimilar to themselves at the H-2 loci than with similar individuals. Such negative assortative mating with respect to H-2 is mediated by olfaction. There are three adaptive hypotheses for MHC-dependent mate choice. First, offspring of individuals that mate disassortatively will tend to be MHC-heterozygotes that may have enhanced immunocompetence. Second, offspring from MHC-disassortative mating are likely to be dissimilar from their parents at MHC loci and this may provide a "moving target" to parasites that adapt to their host's genotype. Third, negative assortative mating with respect to MHC leads to the avoidance of inbreeding. Recently, it has been suggested that human mate choice may be affected by HLA, based on the finding that women prefer the odor of men dissimilar to themselves at HLA loci to that of HLA-similar men. If these odor preferences are indeed an important criterion of mate choice in humans, actual marriages may show negative assortment with respect to HLA. Three recent attempts to detect HLA-disassortative mating in the Hutterites, South Amerindians, and Japanese by examining HLA dissimilarity between spouses have produced mixed results. These studies are reviewed and the disparity among them is discussed.

Major Histocompatibility Complex

MHC (major histocompatibility complex) plays an important role in the immune system (Klein 1986). MHC molecules project out from the cell surface and have a "pocket" on the distal end that binds a small peptide fragment. The shape of the pocket determines which peptide is likely to be bound. The principal function of MHC molecules is to present such

a peptide fragment to T-cells. If the peptide is from nonself, T-cells initiate an immune response. MHC was discovered originally as the major determinant of histocompatibility (required for successful tissue transplantation). The human and mouse MHCs have been studied intensively and are called HLA (human leukocyte antigen) and H-2, respectively.

There are a large number of alleles at each of the MHC loci and this produces so many different combinations that virtually no two individuals are identical in their multilocus MHC genotype. Although the mechanism maintaining such a high degree of polymorphism is not definitely known, natural selection is thought to play a role. Two modes of natural selection that can maintain genetic polymorphism at each locus have been suggested. (1) Overdominant selection: When the heterozygote (Aa, say) has a higher fitness than the homozygotes (AA and aa, say), both alleles (i.e., A and a) are maintained. MHC-heterozygotes may be able to deal with a wider range of antigens. If so, MHC-heterozygotes may have a higher fitness than MHC-homozygotes. Evidence for overdominant selection at the MHC loci has been found at the molecular level (e.g., Hughes & Nei 1988). (2) Frequency-dependent selection: If each allele is more advantageous when rare than common, polymorphism will be maintained. Parasites that can evade a common MHC genotype (both homologous genes are common alleles) increase rapidly. Consequently, a rare MHC genotype (at least one homologous gene is a rare allele) may be more resistant to parasites than a common MHC type and gradually increase its frequency in the population. Such an interaction between hosts and parasites is often referred to as a "coevolutionary arms race." These arguments may be also applied to multilocus MHC haplotypes because the MHC loci are closely linked so that combinations of alleles at different loci are conserved through generations.

MHC-Disassortative Mating in Mice

Mate choice in house mice (*Mus musculus domesticus*) is influenced by MHC (or H-2). Yamazaki et al. (1976) conducted a mate choice experiment using three pairs of mouse strains that are genetically identical except for the H-2 region (i.e., H-2 congenic strains). They observed a male mouse caged with two H-2-congenic female mice in estrus, one similar and the other dissimilar to the male at the H-2, until copulation occurred with one of the two females. In four of the six strains, male mice were more likely to mate with H-2-dissimilar females than with H-2-similar females. Subsequent studies by Yamazaki and his colleagues have confirmed such disassortative (or negative assortative) mating with respect to H-2 (Yamazaki et al. 1978; Yamazaki et al. 1988; Beauchamp et al. 1988; reviewed in Penn & Potts 1999).

Egid and Brown (1989), using a different pair of H-2 congenic strains, demonstrated female mating preferences for H-2-dissimilar males in a mate choice experiment in which a female was allowed to choose between two tethered males. Furthermore, they showed that

H-2-dependent mate choice is mediated by olfaction as described below (see also Yamazaki et al. 1979; reviewed in Penn & Potts 1998a). They investigated female responses to odor of males from congenic strains. A female was introduced into a Y-maze in which each arm of the maze received odors from the soiled bedding of males whose H-2 types were the same as or different from the female. Then the amount of time the female spent in each arm of the Y-maze in a fifteen-min trial was recorded. It turned out that estrous females spent more time near the odor of H-2-dissimilar males than the odor of H-2-identical males. By contrast, Eklund et al. (1991) did not find any evidence of male mating preferences for H-2-dissimilar females with the same congenic strains and experimental design except for sex. This suggests that it may really have been the females who were choosing their mates in the series of experiments performed by Yamazaki and co-workers. That is, males may have mated with H-2-dissimilar females merely because these females were more receptive.

Potts et al. (1991) studied mating patterns in seminatural populations of mice in large enclosures. The mice were derived from crossing wild-caught individuals with four inbred strains carrying known H-2 haplotypes. H-2 genotype frequencies at the embryo and nestling stages in the progeny born in the enclosures were compared with the genotype frequencies expected from random mating. Potts et al. observed a deficiency of H-2 homozygous progeny in all of nine populations studied. This was not due to differential neonatal mortality or selective fertility, because the proportion of homozygotes did not decline between the embryo and nestling stages, and informative laboratory matings did not produce a deficiency of homozygotes. They concluded, therefore, this could be explained only by H-2-disassortative mating.

To mate disassortatively, individual mice require a referent with which to compare the H-2 type of potential mates. Yamazaki et al. (1988) suggested that mice learn the MHC identity of their family during early ontogeny (i.e., familial imprinting). They removed entire litters of mice at birth from their natural parents and reared them with foster parents. Then the mating preferences of the fostered males were investigated by a mate choice experiment as previously described (Yamazaki et al. 1976). Males who had been fostered by H-2-identical parents preferred H-2-dissimilar females. On the other hand, males who had been fostered by H-2-congenic parents tended to mate with females whose H-2 types were different from their foster parents, even when this led to mating with H-2-identical females. Other studies in both laboratory (Beauchamp et al. 1988; Eklund 1997) and seminatural conditions (Penn & Potts 1998b) also indicate familial imprinting.

It should be noted that not all studies support H-2-disassortative mating. Nevertheless, Penn and Potts (1999) mention some reasons to be cautious about overinterpreting negative evidence, including low statistical power as a result of small sample sizes and artificial selection against inbreeding avoiding behavior in the process of domestication.

Adaptive Significance of MHC-Dependent Mate Choice

Three hypotheses have been proposed to explain the function of MHC-dependent mating preferences (Penn & Potts 1999). First, offspring of individuals that mate disassortatively will tend to be heterozygous at MHC loci. If MHC-heterozygotes have a higher fitness than homozygotes, these individuals may have the advantage of having a greater number of surviving offspring. Note that the study by Potts et al. (1991) does not rule out overdominant selection occurring after the nestling stage. Second, offspring from MHC-disassortative mating are likely to be dissimilar from their parents at MHC loci. If MHC diversity is maintained by coevolutionary arms race between hosts and parasites, this may provide a "moving target" to parasites that adapt to their host's genotype. Third, since MHC genes are highly polymorphic, two individuals similar to each other at MHC loci are likely to be relatives (reviewed in Brown & Eklund 1994). Hence, negative assortative mating with respect to MHC promotes the avoidance of deleterious inbreeding.

MHC-Dependent Odor Preferences in Humans

Wedekind et al. (1995) showed experimentally that both body odor and odor preferences in humans are influenced by MHC (or HLA). They typed 49 female and 44 male students at the University of Bern for the HLA-A, -B, and -DR loci. A t-shirt was provided to each of the men and they wore the t-shirts for two consecutive nights. During these two days, they were asked to live as much as possible "odor-neutral." Then the women, who had been asked to prepare themselves for the experiment by taking care of their sense of smell, scored the odor of the t-shirts worn by the men for intensity, pleasantness, and sexiness. Each woman rated six t-shirts, three of them worn by men who were dissimilar to herself at the HLA loci, and three worn by men similar to herself.

The women in the study found the odor of the t-shirts worn by the HLA-dissimilar men to be more pleasant and sexy than the odor of the t-shirts worn by the HLA-similar men. Interestingly, the scores of odor pleasantness were reversed when the women were using oral contraceptives. Wedekind et al. suggested that since contraceptives imitate pregnancy, pregnant women might prefer the odors that are similar to those of relatives. They also showed that the odor of HLA-dissimilar men reminded the women more often of their current or previous mates than did the odor of HLA-similar men, suggesting that HLA-dependent odor preferences influence actual mate choice.

A more recent study using a somewhat different experimental design basically replicated these findings (Wedekind & Füri 1997). In this second study, 58 women and 63 men rated the odor of t-shirts worn by two women and four men. Hence, in contrast to the first study, all participants rated the same six odors. When rated by men or women who were not using oral contraceptives, the score of pleasantness was negatively correlated with the

number of shared alleles at the HLA-A, -B, and -DR loci between the rater and t-shirt-wearer. Women using contraceptives showed, on the other hand, a positive but nonsignificant correlation between pleasantness and HLA similarity. Wedekind & Füri also showed that when odors reminded raters of their actual or former mates, the raters shared less HLA alleles with the t-shirt-wearers than expected by chance.

As Hedrick and Loeschcke (1996) pointed out, Wedekind et al. (1995) did not show any measures of the experimental error, which could have been obtained if the same t-shirt had been presented more than once to the same rater. As a matter of fact, two of the four male t-shirt-wearers and 40 of the 58 female raters in the second study were also included in the first study, giving 18 combinations of odors and raters that occurred in the both studies. For these 18 cases, the scores for pleasantness or intensity were not consistent across the two studies, and the same memory associations were not observed when sniffing the same odor. Wedekind & Füri (1997) argued, however, that this could not be interpreted as a lack of repeatability of the study because these 18 combinations are only a small fraction of all combinations in the study, 294. It would certainly be worthwhile to investigate the repeatability of the "t-shirts study," although there is no reason to suspect low repeatability would create spurious correlations.

MHC Dissimilarity between Spouses

A recent survey has reported the importance of olfactory information in human mate choice (Hertz & Cahill 1997). If the odor preferences claimed by Wedekind and his colleagues are reflected in actual mate choice, negative assortative mating with respect to HLA may be detected by examining the association of HLA types between spouses. There are three recent attempts to detect such negative assortative mating.

Ober et al. (1997) examined similarity between spouses at HLA in the Hutterites, a North American, reproductively isolated, religious group of European ancestry, notable for their large sibships, communal lifestyle, and limited number of HLA haplotypes. They studied 31 (70 percent) of the 44 Hutterite colonies in South Dakota, which were derived from four ancestral colonies. These four lines of descendant colonies are called "lineages" (A-D). Of 545 married couples in the 31 colonies, 411 (75 percent) couples were typed for five-locus haplotypes (HLA-A, -C, -B, -DR, and -DQ).

Marriages among Hutterites are not arranged. Nevertheless, many marriages are endogamous with respect to colony lineage (Table 1). For each of the 15 categories of mating shown in Table 1, Ober et al. separately calculated the numbers of couples expected from random mating that would share one or two haplotypes. Since genotype frequencies were different among the four lineages, the expected values were obtained based on male genotype frequencies in the husband's lineage and female genotype frequencies in the wife's lineage, instead of the average genotype frequencies in the whole population. There were 44

couples that share one or two haplotypes. This was significantly fewer than the expected number, 64.76 (χ^2 = 7.90; df = 1; P = .005). Hence negative assortative mating with respect to HLA was supported in the Hutterites.

Table 1

Lineages at birth for 411 husband-wife couples.

Wife's lineage	Husband's lineage A	B	C	D	Total
A	115(60)	33	24	14	186
B	35	33(26)	10	0	78
C	43	19	42(24)	1	105
D	13	5	8	16(12)	42
Total	206	90	84	31	411

Numbers in parentheses are number of marriages in which partners were born into the same colony. From Ober et al. (1997).

Table 2

Observed and expected numbers of matings that share or do not share alleles at HLA-A, in 11 tribes.

Tribe	Number of matings that share no alleles		one allele		two alleles		N
Tiriyo	5	(6.63)	12	(10.47)	2	(1.89)	19
Waiapi	3	(4.60)	17	(15.76)	5	(4.64)	25
Apalai	0	(1.40)	15	(13.80)	5	(4.80)	20
Urubu-Kaapor	6	(8.22)	14	(14.48)	7	(4.30)	27
Asurini Trocara	6	(3.63)	9	(11.37)	4	(4.00)	19
Arara	2	(1.00)	6	(6.40)	2	(2.60)	10
Paranana Velho	0	(2.50)	19	(14.36)	3	(5.14)	22
Xikrin	1	(1.27)	9	(7.27)	1	(2.45)	11
Mundurucu	3	(2.40)	12	(9.47)	0	(3.13)	15
Karitiana	1	(1.00)	7	(8.31)	5	(3.69)	13
Cinta Larga	2	(2.92)	8	(7.85)	3	(2.23)	13
Total*	29	(35.57)	128	(119.54)	37	(38.87)	194

* χ^2 =1.90, df = 2, NS.

Numbers in parentheses are expectations under random mating. N is total number of matings. From Hedrick & Black (1997).

Furthermore, it was found that, when the couple share a haplotype, the matched haplotype was more likely to be inherited from the fathers than from the mothers, suggesting greater avoidance of maternally (as opposed to paternally) inherited matched haplotypes. Ober et al. argues that this is consistent with the hypothesis that HLA-dependent mating preferences are determined by chemosensory imprinting in early life.

Hedrick and Black (1997) studied 194 couples from eleven South Amerindian tribes of the lower Amazon basin. There is no known history of exchange between these groups. They typed 194 couples who had offspring for HLA-A and -B loci. The couples sampled constitute a considerable portion of the couples with children in ten of the eleven tribes (52 percent on average). The level of polymorphism was low (four alleles for HLA-A and five

alleles for HLA-B) relative to most African, Asian, and European populations.

The couples were classified into three categories according to the number of shared alleles, that is, couples that share no alleles, one allele, or two alleles for a given locus. The random expectation for each of the categories was calculated separately for each tribe, using male and female genotype frequencies in the tribe. Table 2 shows the observed and expected numbers of matings that share no, one, or two alleles at HLA-A. Total number of matings for each category were not different from expected. The result was essentially the same at the HLA-B locus. Overall, no evidence of HLA-disassortative mating was found in South Amerindians.

In fact, for both loci, there was a slight deficiency of matings that share no alleles, which is contrary to what would be predicted by disassortative mating. A possible factor that would increase sharing of HLA alleles between spouses is a socially dictated preference for cross-cousin marriages, which is known in some Amerindians. Hedrick and Black stated, however, that only a small minority of the eleven tribes in the study appeared to have such preferences and concluded that such cultural preferences are unlikely to mask a substantial effect due to HLA-dependent mating preferences.

We examined the hypothesis of HLA-disassortative mating in two samples of Japanese couples (Ihara et al. 2000). The first sample, which is called "Tohoku," includes 154 married couples from six prefectures in the Tohoku region of Japan (Takahashi et al. 1992). The couples were typed for five-locus haplotypes (HLA-A, -C, -B, -DR, and -DQ). The subjects that constituted the second sample, "8JW", were 291 married couples from sixteen prefectures all over Japan and typed for four-locus haplotypes (HLA-A, -C, -B, and -DR) (see Fujii et al. 1983).

Marital associations at HLA loci were examined for each individual locus and for

Table 3

Number of matings that share HLA alleles or haplotypes in Tohoku and 8JW.

		Number of matings that share							
Sample	Locus	no alleles		one allele		two alleles		N	G
Tohoku	A	56	(58.75)	87	(82.06)	11	(13.19)	154	0.81
	C	58	(62.73)	84	(79.12)	11	(11.16)	153	0.66
	B	109	(111.95)	42	(40.16)	3	(1.89)	154	0.72
	DR	87	(95.53)	59	(52.07)	5	(3.40)	151	2.33
	DQ	47	(53.24)	87	(81.21)	17	(16.55)	151	1.18
	Haplotype	138	(141.84)	9	(6.07)	1	(0.08)	148	4.52*
8JW	A	114	(107.67)	148	(158.11)	29	(25.21)	291	1.57
	C	95	(96.37)	163	(153.67)	24	(31.96)	282	2.74
	B	206	(203.77)	72	(74.77)	4	(3.46)	282	0.21
	DR	95	(98.37)	78	(77.95)	11	(7.68)	184	1.38
	Haplotype	131	(133.96)	12	(8.92)	0	(0.12)	143	1.26

Numbers in parentheses are expectations under random mating. N is total number of matings. *$P < 0.05$ based on 2000 simulations. Modified from Ihara et al. (2000).

haplotypes. The couples were classified into three categories according to the number of shared alleles/haplotypes in the same manner as Hedrick and Black (1997). Expected numbers were calculated on the basis of observed male and female genotype frequencies in each sample as a whole. Table 3 shows numbers of matings that share no, one, or two alleles/haplotypes in each sample.

For each test of random mating, we used an empirical distribution of G-statistic obtained by a Monte Carlo method, since the distribution of G under the null hypothesis cannot a priori be assumed as usual to follow the chi-square distribution with 2 degrees of freedom. Only for the five-locus haplotypes in Tohoku was there a statistically significant deviation from random mating. Observed mean number of shared haplotypes was, however, greater than expected. This result may reflect positive assortative mating, but it is more likely attributable to population structure in the area. In fact, genotype frequencies for HLA-B, HLA-DR, and haplotypes were heterogeneous among prefectures in both samples. Hence it is possible that disassortative mating at the prefectural level was masked in the above tests. To minimize this effect, tests of random mating were also performed for each prefecture in both samples. To be brief, random mating was not rejected by these tests. However, estimated statistical power of these tests was low because of small sample size.

In sum, we can rule out strong disassortative mating at the HLA-A and HLA-C loci, since for these loci statistical power was relatively high and population structure was not detected. Although the power of the statistical tests were often too low to permit a definitive conclusion to be reached, we could not find any evidence of disassortative mating in Japanese couples at any of the loci examined or for haplotypes.

Do Humans Mate Disassortatively with Respect to MHC?

Ober et al. (1997) is the only study to date that has demonstrated negative assortative mating with respect to HLA. Since the two other studies (Hedrick & Black 1997; Ihara et al. 2000) did not find evidence of negative assortment (see also Pollack et al. 1982; Rosenberg et al. 1983; Jin et al. 1995), the results of Ober et al. should be viewed with caution. On the other hand, there may be good reasons why Ober et al. (1997) "succeeded."

First, Ober et al. (1997) took population structure into account. Since the Hutterites are endogamous with respect to colony lineage, it would have been misleading if they had calculated the expectations based on genotype frequencies throughout the population. Fortunately, they had a complete knowledge of the birthplaces of the subjects so that they could calculate the expectations based on male genotype frequencies in the husband's lineage and female genotype frequencies in the wife's lineage. Ihara et al. (2000), also aware of population structure but lacking information about the subjects' birthplaces, conducted instead tests of random mating separately for each prefecture to minimize the effect of population structure. However, statistical power of these tests was low as a result of reduced

sample size.

Second, the level of HLA polymorphism in the Hutterites is low. Ober et al. (1997) found only 59 five-locus haplotypes by serology or by DNA typing, while Ihara et al. (2000) observed 326 in the Tohoku sample by serology. Although Hedrick and Black (1997) did not type five-locus haplotypes, the haplotype diversity in the studied populations is likely to be low since there were only four alleles at HLA-A and five alleles at HLA-B by serology. Both Ober et al. (1997) and Hedrick and Black (1997) note that HLA-disassortative mating might be detectable only in populations with a low level of HLA polymorphism. This argument is supported by Ihara et al. (2000), which showed that statistical power of tests for random mating was the highest when conducted with respect to the HLA-A, -C, or -DQ loci, at which the number of alleles were the fewest.

Third, the Hutterite society is notably homogenous in factors that could potentially influence human mate choice, such as social status, education, income, and ethnicity (Ober et al. 1997; see Hostetler & Huntington 1980). The influence of HLA on mate choice would be weakened, if not counterbalanced, in more heterogeneous societies because people use many criteria other than HLA similarity when they choose their mates (e.g. Buss 1989). Hence, it is supposed that the more heterogeneous a studied society is, the larger the sample is required to be to detect HLA-disassortative mating.

Fourth, Ober et al. (1997) is a large study. They sampled 411 couples while Hedrick and Black (1997) sampled 194. The sample of Ihara et al. (2000) is also large (445 couples in total), but suffers from the limitations noted above.

With hindsight, Ober et al. (1997) is perhaps the only study to date that stood a chance of demonstrating negative assortative mating with respect to HLA, given that the phenomenon occurs. Taken together, I have to put off answering the above question at the moment. Further study is clearly warranted, particularly with a large sample collected from a socially homogeneous population that has relatively low genetic variability and with a precisely known structure.

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References

Beauchamp, G. K., Yamazaki, K., Bard, J., & Boyse, E. A.

1988. Preweaning experience in the control of mating preferences by genes in the major histocompatibility complex of the mouse. *Behavior Genetics* 18: 537-547.

Brown, J. L. & Eklund, A.

1994. Kin recognition and the major histocompatibility complex: An integrative review.

The American Naturalist 143: 435-461.

Buss, D. M.

1989. Sex differences in human mate preferences: Evolutionary hypotheses tested in 37 cultures. *Behavioral and Brain Sciences* 12: 1-49.

Egid, K. & Brown, J. L.

1989. The major histocompatibility complex and female mating preferences in mice. *Animal Behaviour* 38: 548-550.

Eklund, A.

1997. The effect of early experience on MHC-based mate preferences in two B10.W strains of mice (*Mus domesticus*). *Behavior Genetics* 27: 223-229.

Eklund, A., Egid, K., & Brown, J. L.

1991. The major histocompatibility complex and mating preferences of male mice. *Animal Behaviour* 42: 693-694.

Fujii, Y., Juji, T., & Kaihara, S.

1983. Family study of HLA-A, B, C, and DR in Japanese. *Japanese Journal of Transplantation* 18: 189-203 [In Japanese].

Hedrick, P. W. & Black, F. L.

1997. HLA and mate selection: No evidence in South Amerindians. *American Journal of Human Genetics* 61: 505-511.

Hedrick, P. W. & Loeschcke, V.

1996. MHC and mate selection in humans? *Trends in Ecology and Evolution* 11: 24.

Hertz, R. S. & Cahill, E. D.

1997. Differential use of sensory information in sexual behavior as a function of gender. *Human Nature* 8: 275-286.

Hostetler, J. A. & Huntington, G. E.

1980. *The Hutterites in North America.* New York: Holt, Rinehart, and Winston.

Hughes, A. L. & Nei, M.

1988. Pattern of nucleotide substitution at major histocompatibility complex class I loci reveals overdominant selection. *Nature* 335: 167-170.

Ihara, Y., Aoki, K., Tokunaga, K., Takahashi, K., & Juji, T.

2000. HLA and human mate choice: Tests on Japanese couples. *Anthropological Science* 108: 199-214.

Jin, K., Speed, T. P., & Thomson, G.

1995. Tests of random mating for a highly polymorphic locus: Application to HLA data. *Biometrics* 51: 1064-1076.

Klein, J.

1986. *Natural History of the Major Histocompatibility Complex.* New York: Wiley.

Ober, C., Weitkamp, L. R., Cox, N., Dytch, H., Kostyu, D., & Elias, S.

1997. HLA and mate choice in humans. *American Journal of Human Genetics* 61: 497-504.

Penn, D. J. & Potts, W. K.

1998a. How do major histocompatibility complex genes influence odor and mating preferences? *Advances in Immunology* 69: 411-436.

Penn, D. J. & Potts, W. K.

1998b. MHC-disassortative mating preferences reversed by cross-fostering. *Proceedings of the Royal Society of London, Series B*, 265: 1299-1306.

Penn, D. J. & Potts, W. K.

1999. The evolution of mating preferences and major histocompatibility complex genes. *The American Naturalist* 153: 145-164.

Pollack, M. S., Wysocki, C. J., Beauchamp, G. K., Braun, D. Jr., Callaway, C., & Dupont, B.

1982. Absence of HLA association or linkage for variations in sensitivity to the odor androstenone. *Immunogenetics* 15: 579-589.

Potts, W. K., Manning, C. J., & Wakeland, E. K.

1991. Mating patterns in seminatural populations of mice influenced by MHC genotype. *Nature* 352: 619-621.

Rosenberg, L. T., Cooperman, D., & Payne, R.

1983. HLA and mate selection. *Immunogenetics* 17: 89-93.

Takahashi, K., Tokunaga, K., Uchikawa, C., Juji, T., Akaza, T., Umezawa, K., Endoh, N., Kamata, H., Tsuchida, H., Fujino, K., & Watanabe, I.

1992. Evaluation of an appropriate size of unrelated donor pool for HLA-matched platelet transfusion and bone marrow transplantation. *Japanese Journal of Transfusion Medicine* 38: 475-481 [In Japanese].

Wedekind, C., Seebeck, T., Bettens, F., & Paepke, A. J.

1995. MHC-dependent mate preferences in humans. *Proceedings of the Royal Society of London, Series B*, 260: 245-249.

Wedekind, C. & Füri, S.

1997. Body odor preferences in men and women: Do they aim for specific MHC combinations or simply heterozygosity? *Proceedings of the Royal Society of London, Series B*, 264: 1471-1479.

Yamazaki, K., Beauchamp, G. K., Kupniewski, D., Bard, J., Thomas, L., & Boyse, E. A.

1988. Familial imprinting determines H-2 selective mating preferences. *Science* 240: 1331-1332.

Yamazaki, K., Boyse, E. A., Mike, V., Thaler, H. T., Mathieson, B. J., Abbott, J., Boyse, J., Zayas, Z. A., & Thomas, L.

1976. Control of mating preferences in mice by genes in the major histocompatibility complex. *The Journal of Experimental Medicine* 144: 1324-1335.

Yamazaki, K., Yamaguchi, M., Andrews, P. W., Peake, B., & Boyse, E. A.

1978. Mating preferences of F2 segregants of crosses between MHC-congenic mouse strains. *Immunogenetics* 6: 253-259.

Yamazaki, K., Yamaguchi, M., Baranoski, L., Bard, J., Boyse, E. A., & Thomas, L.

1979. Recognition among mice: Evidence from the use of a Y-maze differentially scented by congenic mice of different major histocompatibility types. *The Journal of Experimental Medicine* 150: 755-760.