Letters to the Editor

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HLA and Mate Choice

To the Editor:

The papers on HLA and mate choice, by Hedrick and Black (1997), who studied South Amerindian tribes, and by Ober et al. (1997), who studied the relatively closed and partially inbred Hutterite populations, as well as the invited editorial by Beauchamp and Yamazaki (1997), point out the conflicting evidence for this potential relationship and some of the possible reasons for it. I would like to suggest an alternative approach.

My colleagues and I have shown that there is a relationship between recurrent spontaneous abortion and genes linked to HLA-DR and between unexplained infertility and genes linked to HLA-DQ (Gill 1992; Jin et al. 1995). It is important to note that the data showed that genes *linked* to the genes encoding HLA antigens—and not the HLA genes themselves—are involved in these associations between HLA and reproductive defects. The same conclusion has been proposed for the association between HLA and susceptibility to rheumatoid arthritis (Dizier et al. 1993), between HLA-DR and HLA-DQ and insulin-dependent diabetes mellitus (Clerget-Darpoux et al. 1991; Dizier et al. 1994), and between HLA and multiple sclerosis (Francis et al. 1991).

I propose that the potential association between HLA and mate selection may reside in the HLA-B–DR-DQ region and that this association should be explored in detail. Inclusion of the HLA-A locus in the analysis can obscure this potential effect considerably (Ho et al. 1994). Hedrick and Black (1997) typed only for HLA-A and HLA-B, and Ober et al. (1997) did not give the details of the genetic structure of the haplotypes in the various mating combinations. The latter group, however, has published on the relationship between HLA-DR and fertilization or implantation in the same Hutterite populations (Ober et al. 1992; Ober 1995); thus, it seems reasonable that, if mate selection has an association with genes in the HLA complex, these genes may reside in the HLA-B–DR-DQ region.

If a relationship between the major histocompatibility

complex (MHC) and mate selection is borne out in humans, it may reflect an evolutionary reproductive drive to avoid homozygosity for MHC-linked recessive reproductive genetic defects (Gill 1997a, 1997b). It is interesting to speculate that this type of evolutionary drive may also be the basis for the near-universal human taboo against incest.

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References

Beauchamp GK, Yamazaki K (1997) HLA and mate selection in humans: commentary. Am J Hum Genet 61:494–496

Clerget-Darpoux F, Babron MC, Deschamps I, Hors J (1991) Complementation and maternal effect in insulin-dependent diabetes. Am J Hum Genet 49:42–48

Dizier M-H, Babron M-C, Clerget-Darpoux F (1994) Interactive effect of two candidate genes in a disease: extension of the marker-association-segregation χ^2 method. Am J Hum Genet 55:1042–1049

Dizier M-H, Eliaou J-F, Babron M-C, Combe B, Sany J, Clot J, Clerget-Darpoux F (1993) Investigation of the HLA component involved in rheumatoid arthritis (RA) by using the marker association–segregation χ^2 (MASC) method: rejection of the unifying-shared-epitope hypothesis. Am J Hum Genet 53:715–721

Francis DA, Thompson AJ, Brookes P, Davey N, Lechler RI, McDonald WI, Batchelor JR (1991) Multpile sclerosis and HLA: is the susceptibility gene really HLA-DR or -DQ? Hum Immunol 32:119–124

Gill TJ III (1992) Influence of MHC and MHC-linked genes on reproduction. Am J Hum Genet 50:1–5

——— (1997a) Genetic factors in reproduction and their evolutionary significance. Am J Reprod Immunol 37:7–16

——— (1997b) Genetics of reproduction and its role in evolution. Periodicum Biologorum 99:289–294

Hedrick PW, Black FL (1997) HLA and mate selection: no evidence in South Amerindians. Am J Hum Genet 61: 505–511

Ho H-N, Yang Y-S, Hsieh R-P, Lin H-R, Chen, S-U, Chen H-F, Huang S-C, et al (1994) Sharing of human leukocyte antigens in couples with unexplained infertility affects the success of in vitro fertilization and tubal embryo transfer. Am J Obstet Gynecol 170:63–71

- Jin K, Ho H-N, Speed TP, Gill TJ III (1995) Reproductive failure and the major histocompatibility complex. Am J Hum Genet 56:1456–1467
- Ober C (1995) HLA and reproduction: lessons from studies in the Hutterites. Placenta 16:569–577
- Ober C, Elias S, Kostyu DD, Hauck WW (1992) Decreased fecundability in Hutterite couples sharing HLA-DR. Am J Hum Genet 50:6–14
- Ober C, Weitkamp LR, Cox N, Dytch H, Kostyu D, Elias S (1997) HLA and mate choice in humans. Am J Hum Genet 61:497–504

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