haplotype frequencies for HLA-A, HLA-B, HLA-DR and to disregard for the calculations the alleles of the loci HLA-C, as well as of HLA-DQA1 and of HLA-DQB1, which show very strong positive gametic associations with HLA-B and HLA-DR alleles, respectively. Analogous considerations are valid for all the genetic systems built up by several closely linked loci coding for alleles in strong linkage disequilibrium, e.g., many of the recently described DNA polymorphisms.

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Reply to Mayr

To the Editor:

We agree with Dr. Mayr that for linked genes that are in strong linkage disequilibrium haplotype frequencies rather than the products of individual phenotype frequencies should be used to calculate probabilities used in parentage evaluation (e.g., P^E). Our paper addressed the population genetics of the HLA-DQA1 locus, as detected by a PCR-based method; the application to paternity testing was presented as a single, independent genetic system. The existence of linkage disequilibrium between loci in the HLA region is, of course, well-known; however, the strength of the disequilibrium varies significantly between different locus pairs. The example given by Dr. Mayr involves DR and DQ alleles known to be in very strong linkage disequilibrium. On the basis of the analysis of CEPH pedigrees, the HLA-DQA1 alleles, however, are in much weaker linkage disequilibrium with the telomeric HLA-B and HLA-A loci and with the centromeric HLA-DPB1 locus. For these markers, the difference between using haplotype and allele frequencies is substantially less than in the example given by Dr. Mayr. A paper that describes recombination frequencies and allele and haplotype frequencies and that uses PCR-based HLA typing of the CEPH pedigrees to estimate linkage disequilibrium between HLA loci is currently in preparation.

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A Novel Approach to Establishing Permanent Lymphoblastoid Cell Lines: Epstein-Barr Virus Transformation of Cryopreserved Lymphocytes

To the Editor:

A practical limitation of human genetic analysis has been the logistical difficulty of shipping fresh blood samples from field sites to the laboratory quickly enough that transformation by Epstein-Barr virus (EBV) can be accomplished. Because we also confronted this problem, we developed a procedure for freezing cells and subsequent thawing and EBV transformation. The portion of the protocol for freezing cells can easily be carried out in many clinical facilities; then frozen aliquots can be carried or shipped when convenient to a laboratory capable of transformation.

An additional advantage of freezing prior to transformation is that one can sample persons who may or may not ultimately be crucial to genetic analysis, easily freeze and store lymphocytes, and then decide subsequently which samples should be immortalized.