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LETTERS

NRC Report on DNA Typing

In their letter of 23 April (p. 473) concerning our critique (Policy Forum, 5 Feb., p. 748) of the National Research Council's (NRC's) report on DNA typing (*1*), Daniel L. Hartl and Richard C. Lewontin say that we "assert that deciding whether or not the multiplication rule should be used as evidence in court 'remains the venue of legal scholars, not population geneticists or statisticians.' " What we said was that, compared with statistically based methods (*2*), the methods currently used in court and those recommended by the NRC report were both conservative, the latter more conservative than the former. Then we noted that the degree of conservativeness remains the venue of legal scholars. Hartl and Lewontin also say that we say we are "against additional research to obtain data relevant to population substructure" and call for "no new data." What we said was that the proposed study was so poorly designed it would not resolve any outstanding population genetic questions. The critical flaw is the small number of individuals to be sampled per subpopulation (*3*). While we have no objections to new data from a properly designed study (which would require much larger sample sizes), we do not anticipate that such a study would lead to a conclusion other than that the current methods of estimating genotype probabilities are already conservative.

We stand by our claim of consensus within the relevant scientific community: the Taylor-made "informal telephone survey," mentioned by Hartl and Lewontin, being neither random nor unbiased, would not be taken seriously by statisticians and has had no effect on admissibility decisions (*4*). As we have said, those who have performed thorough analyses of variable number of tandem repeat (VNTR) databases are satisfied that the methods used in court are generally conservative.

Regarding the issue of gene diversity between ethnic groups (or races) and between subpopulations within ethnic groups, the facts are immutable. Lewontin's estimates of subpopulation and ethnic diversity were 8.3% and 6.3%, respectively (*5*). Hartl and Lewontin (*6*) used this result to argue against the validity of standard methods of calculating genotype probabilities because "there is, on average, one-third more genetic variation among Irish, Spanish, Italians, Slavs, Swedes, and other subpopulations, than there is, on the average, between Europeans, Asians, Africans, Amerinds, and Oceanians." In our critique, we cited a number of articles that came to a different conclusion. Now, instead, Hartl and Lewontin say that Lewontin stated that "there is approximately as much genetic variation among [subpopulations] as there is among [ethnic groups]." That is not the point: both Hartl and Lewontin (*6*) and the NRC report said there is much greater variation among subpopulations than among ethnic groups, thus motivating the NRC report's "ceiling principle."

In Hartl and Lewontin's discussion of Latter's study (*7*), part of which essentially duplicated Lewontin's research with larger samples, they say, "Latter uses three different methods of estimating the variation between [ethnic groups] and between [subpopulations], one of which is the same as Lewontin's [(*5*)]. Latter's three sets of values are 0.104:0.056, 0.075:0.055, and 0.096:0.066. These values should be compared with Lewontin's values of 0.063:0.083." In fact, only one (0.104:0.056) is directly comparable with Lewontin's. So, for a study based on more loci, more populations, and larger sample sizes, Latter obtained one-half the variation between subpopulations as he did between ethnic groups, whereas Hartl and Lewontin say it was one-third more variation. Part of the explanation for these discrepancies may be statistical. Our theoretical analyses (*3*) indicate that Lewontin's method of partitioning diversity is biased, exaggerating differences among subpopulations relative to ethnic groups.

Furthermore, even Latter's analyses are not completely relevant because they give as much weight to small isolated subpopulations as they do to the large open subpopulations that are a source of most U.S. ethnic groups. Hence one would expect the subpopulation diversity to be even less in U.S. ethnic groups. In this regard, Nei and Roychoudhury (*8*), using heterozygosity, also found that ethnic groups accounted for 9 to 11% of gene diversity, but only 0.5% or less was attributable to differences among English, Germans, and Italians; that is, one-twentieth of the variability as opposed to Hartl and Lewontin's 33% more variability. In industrialized societies like the United States, the estimate of diversity based on variance of allele frequencies among subpopulations is usually quite small—approximately 0.1% (*9*). Studies based on VNTR

loci and U.S. populations find similar values, approximately 0.1% or less (*10, 11*).

Given these facts, how can we explain the "data analyses" presented in Hartl and Lewontin's first paper (6) and the new "analyses" by Hartl and his colleagues (*12*)? We will not belabor Hartl and Lewontin's first analyses (6), which suggested large differences between Poles and Italians. The subsequent analyses by Chakraborty and Kidd (*13*), and more recently by Morton *et al.* (*10*), show that Hartl and Lewontin's results are artifacts of using inappropriate data.

Far more interesting, statistically, are Hartl's results on genotype probabilities (*12*). Hartl and Lewontin argue that these results prove the necessity of the NRC's ceiling principle, but they again appear to be misled by their inadequate data. The data Hartl used were from 1353 U.S. Caucasians (heritage unspecified), 56 Finns, and 78 Italians, although the Finnish and Italian databases contained only 29 and 70 individuals, respectively, with complete three-locus profiles. For each three-locus European profile, profile probabilities were calculated using the database containing the profile (cognate population) and the other database (noncognate population) by assuming independence of alleles within and between loci. Not surprisingly, Hartl found larger probabilities 77% of the time using the cognate database.

These results have a simple, statistical explanation: (i) for small samples, leaving the individual whose profile is to be estimated in the cognate database induces a large upward bias in the estimated probability; and (ii) small samples frequently create spuriously large correlations among the parameter estimates, in this case, the allele probabilities. The effect of the bias is that the genotype will more often have a higher probability in the cognate database than in the noncognate database. The correlations affect the variance of the genotype probability estimates.

These statistical phenomena were recognized by Budowle *et al.* (*14*), who designed an experiment to examine them. These authors sampled profiles from Hartl's large Caucasian database to create artificial "European" populations of the same sample size as Hartl's data for Finns and Italians. They then calculated the profile probabilities, finding profiles were generally more common in the "cognate" database. For 1000 replicate experiments, the profile probability was more common in the cognate database 73.3% of the time on average, with a standard deviation of 4.4%; the maximum value was 85.9%. In contrast, for sampling without replacement, 50:50 proportions obtain. Hence Hartl, and Hartl and Lewontin subsequently, again imbue a statistical artifact with a population genetic meaning and say, "new data demonstrate that the methods currently used in court are not conservative—they are systematically prejudiced against the defendant—and no amount of argument will make them conservative." To the contrary, the new data demonstrate nothing of the kind. In fact, they could be used to argue for the opposite conclusion. Hartl's analyses, however, do prove the point we made earlier in *Science* and will make elsewhere (*3*) about the design of the new study proposed in the NRC report: small sample sizes are inadequate for population genetic inference from VNTRs or other highly polymorphic markers.

From Hartl and Lewontin's letter and their previous writings, one might imagine the following scenario: a DNA profile is obtained at a crime scene in Finland and, although there is no reason to suspect the perpetrator is Italian, an Italian database is used to calculate the profile probability. Such a practice might be reasonable on the other side of the looking glass, but it is not the practice of forensic scientists. Rather, Finnish forensic scientists use Finnish databases. In the ethnically mixed United States there is usually no reason to suppose the heritage of the suspect is similar to that of the perpetrator, at least under the assumption of innocence. In such cases, the profile probability is calculated on the basis of general U.S. ethnic samples. Notably, for such samples, the methods currently in use in court yield conservative profile probabilities, frequently orders of magnitude more conservative than profile probabilities obtained from statistically based methods (*2*). Hartl and Lewontin ignore the consequence of this fact, which is that population substructure would have to be unrealistically large (contrary to evidence) for standard forensic calculations to be seriously in error. Thus, we see no scientific justification for adopting even more conservative methods, as Hartl and Lewontin and the NRC report advocate.

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References

1. Committee on DNA Technology in Forensic Science, *DNA Technology in Forensic Science* (National Academy Press, Washington, DC, 1992).
2. B. Devlin, N. Risch, K. Roeder, *J. Am. Stat. Assoc.* **87**, 337 (1992); D. A. Berry, I. W. Evett, R. Pinchin, *Appl. Stat.* **41**, 449 (1992); I. W. Evett, J. Scrange, R. Pinchin, *Am. J. Hum. Genet.* **52**, 498 (1993).
3. B. Devlin, N. Risch, K. Roeder, *J. Forensic Sci.*, in press.

4. *People* v. *Donald Menephee*, Los Angeles County Superior Court, docket LA 003 852, decided 8 July 1991.
5. R. C. Lewontin, *Evol. Biol.* **6**, 381 (1972).
6. _____ and D. L. Hartl, *Science* **254**, 1745 (1991).
7. B. D. H. Latter, *Am. Nat.* **116**, 220 (1980).
8. M. Nei and A. K. Roychoudhury, *Evol. Biol.* **14**, 1 (1982).
9. N. Morton, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 2556 (1992).
10. N. Morton, A. Collins, I. Balazs, *ibid.* **90**, 1892 (1993).
11. M. Escobar, J. Kadane, K. Roeder, in preparation; R. Chakraborty, in preparation.
12. D. E. Krane, R. W. Allen, S. A. Sawyer, D. A. Petrov, D. L. Hartl, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 10583 (1992).
13. R. Chakraborty and K. K. Kidd, *Science* **254**, 1735 (1991).
14. B. Budowie, K. Monson, A. Giusti, in preparation.

In responding to Devlin *et al.*'s comments about the NRC report (*1*) on DNA technology in forensic science, Hartl and Lewontin make some statements which suggest that they now have a revised opinion with regard to the extent of population substructuring at various levels of human populations. With the rationale that there exist allele frequency differences between populations defined by race or ethnicity, Hartl and Lewontin previously argued (*2*) that the use of the multiplication rule is unwarranted in forensic applications of DNA typing. In arriving at this conclusion, they stated that "there is, on average, one-third more genetic variation among Irish, Spanish, Italians, Slavs, Swedes, and other subpopulations, than there is, on the average, between Europeans, Asians, Africans, Amerinds, and Oceanians" (*2*, p. 1747). In their critique of 5 February, Devlin *et al.* present data to contradict this statement. In their letter of 23 April, Hartl and Lewontin, with citations of the same data, now conclude "that there is approximately as much variation among ethnic groups within major races as there is among the races." A closer examination of their re-analysis (see the preceding sentence of their letter), however, indicates that they now arrive at approximately one-third (1.3:1) more variation among races than that among ethnic groups within major races. This reversal of opinion, combined with the scatter plot shown in figure 1 of (*3*), should be sufficient to illustrate that the effect of population substructuring has little impact on the significance attached to DNA profile match found in forensic case analyses. Specifically, the use of allele frequencies from a database that is diverse from the appropriate reference population results in substantial differences only when, in each of the populations, the DNA profile has a probability on the order of one in several tens of thousands, or smaller. A recent analysis (*4*), with its inherent statistical artifact, cannot be invoked to refute this.

An apportionment analysis also overemphasizes the variance component that results from a level of subdivision when the number of populations within the subdivision is not factored in the analysis (*5*), as was the case in Lewontin's early work (*6*). Furthermore, Hartl and Lewontin, as well as Devlin *et al.*, used data on traditional genetic markers to argue their cases. Their arguments do not strictly apply to U.S. populations, as in this context we need data on regional differences and their effects on forensic computations. Such data existed for traditional loci (*7*), and they are now available for DNA markers as well (*8*). Analysis of these data indicate that the extent of regional difference within a racial group is far less than that between races [for example, analysis of data from (*7*) indicates that, of the total gene diversity in the U.S. population at eight traditional loci, 2.73% can be ascribed to allele frequency differences between two major racial groups, while only 0.37% is caused by differences among regional populations within a racial group (*9*)]. The conclusions from kinship bioassay analysis of hypervariable DNA loci are almost parallel to this finding, namely the mean kinship within race is 0.4% (*10*), as expected. This was predicted earlier from standard population genetic principles (*11*). Mean kinship within populations is a decreasing function of per locus variation; therefore, the observation that kinship within a race is less by an order of magnitude for hypervariable DNA loci than for blood groups and isozymes is in perfect accordance with the predictions of population genetic theory (*11*). With these low levels of kinship, the earlier assertion that genetic differentiation among subgroups has a negligible effect on the multiplication rules (*3*), with which Lewontin and Hartl agree (*12*, p. 1054), still appears to provide adequate justification for the current forensic practice in relation to legal applications of DNA typing. However, this is not a statement of complacency, as studies of variation at hypervariable DNA loci in diverse, anthropologically defined populations are better suited for examining the extent of human population structure. Initial data (*13*) indicate that, even in the midst of substantial allele frequency differences among populations, the hypervariability of interindividual DNA profiles is so great that it dwarfs any interpopulational difference, no matter how crudely or finely populations are defined. As a result, each multilocus DNA genotype is so rare that is forensic significance virtually eliminates the possibility of miscarriage of justice when a match is observed over three or more loci.

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References

1. Committee on DNA Technology in Forensic Science, *DNA Technology in Forensic Science* (National Academy Press, Washington, DC, 1992).
2. R. C. Lewontin and D. L. Hartl, *Science* **254**, 1745 (1991).
3. R. Chakraborty and K. K. Kidd, *Science* **254**, 1735 (1991).
4. D. E. Krane, R. W. Allen, S. A. Sawyer, D. A. Petrov, D. L. Hartl, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 10583 (1991).
5. R. Chakraborty, in *Multivariate Analysis*, P. R. Krishnaiah, Ed. (Elsevier, Amsterdam, 1985), vol. 6, p. 77; see note 26 of B. Devlin, N. Risch, K. Roeder, *Science* **259**, 748 (1993) for other statistical inadequacies of the current apportionment analysis.
6. R. C. Lewontin, *Evol. Biol.* **6**, 381 (1972).
7. B. Cohen *et al.*, *DHEW Publ. No. (PHS) 80-1664* (National Center for Health Statistics, Department of Health, Education, and Welfare, Hyattsville, MD, 1980).
8. Laboratory Division, Federal Bureau of Investigation, *VNTR Population Data: A Worldwide Study*, vols. 1 to 4 (Forensic Science Research and Training Center, Quantico, VA, 1993).
9. R. Chakraborty, in *Modern Human Genetics: A Centennial Tribute to J. B. S. Haldane*, P. P. Majumder, Ed. (Plenum, New York, in press).
10. N. E. Morton, A. Collins, I. Balazs, *Proc. Natl. Acad. Sci. U.S.A.* **90**, 1892 (1993).
11. R. Chakraborty and L. Jin, *Hum. Genet.* **88**, 267 (1992).
12. R. C. Lewontin and D. L. Hartl, *Science* **255**, 1054 (1992).
13. R. Deka, R. Chakraborty, R. E. Ferrell, *Genomics* **11**, 83 (1992); R. Deka *et al.*, *Am. J. Hum. Genet.* **51**, 1325 (1992); R. Chakraborty *et al.*, *Am. J. Hum. Biol.* **4**, 387 (1992).

Interdisciplinary Communication

Jan A. Witkowski suggests (Letters, 9 Apr., p. 147) that although "sociological studies of the way scientists work and how what is regarded as scientific knowledge comes into being are interesting," the "convoluted language" of the packaging self-defeatingly conceals the lessons from scientists; he thus urges sociologists of science to "write more intelligibly." Such a line of reasoning highlights the double standard emerging from Western scientific positivism. It is inevitable that as the problems get more complex so will the language that tries to define them; the concomitance is not the doing of any one group of academicians but is rather an almost necessary consequence of any expanding knowledge base, including that of natural science. Thus, while we may respect the basic postmodern lesson that one's discipline does not exist in a vacuum (something Witkowski himself even does), it remains only historical irony that we still ask others to adapt to us and the subculture where our brand of knowledge feels comfortable. It is *everyone's* responsibility to improve interdisciplinary communication, something that starts and ends with willingness, plenty of patience, and an open mind.

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Evolutionary Relationships

I enjoyed the Random Samples item (16 Apr., p. 295) about the wonderful report by Mitchell Sogin and his colleagues (16 Apr., p. 340) that defines the animal-fungal connection. However, I must carp about the use of the now-outmoded "five-kingdoms" graphic showing evolutionary relationships among lifeforms. Although that view still pervades many textbooks, recent molecular phylogenetic analyses have proved it fundamentally wrong (*1*). "Monera" is not a single relatedness group, but two: Bacteria (formerly eubacteria) and Archaea (formerly archaebacteria), as different from one another as either is from eucaryotes. The eucaryotic *nuclear* line of descent (Eucarya) is not derived from either of the procaryotic groups. Rather, it is as old as either of the other lineages. The incorrect portrayal of these relationships is a step back in the presentation of the remarkable advances that have recently been made in our understanding of biological evolution.

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References

1. C. Woese *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **87**, 4576 (1990).