
Sir,

Analysis of CODIS data from a large study of human populations by Budowle et al. (1) raised concerns articulated in a Commentary by Krane et al. (2) and rebutted in the Authors’ Response by Chakraborty et al. (3). One aspect of this exchange merits additional discussion.

Krane et al. (2) objected to the use of a Bonferroni correction when a test of Hardy-Weinberg equilibrium (HWE) was performed on this dataset. While the original study convincingly demonstrated differentiation among population groups and the absence of structure within individual populations, the use of a Bonferroni correction, as defended in the Response, may be inappropriate. This adjustment has been repeatedly critiqued in recent ecological and evolutionary literature (4–7). Kinnison et al. (8) suggested that if one is interested in testing the combined multilocus evidence of HWE over the entire dataset, as was done in Budowle et al. (1), the binomial likelihood function is more appropriate. As the number of loci and/or populations increases, critical values can become exceptionally small making detection of truly significant results improbable, i.e., inflating type I errors and generating false negatives. This may not be acceptable if the researchers wish to identify multilocus evidence of populations that exhibit structure or multilocus evidence of problematic loci. For example, consider a sample that deviated significantly (p = 0.010) from HWE at each of 12 loci examined. In a general test of HWE using a Bonferroni corrected critical value, such as performed by Budowle et al. (1), these deviations would be deemed inconsequential if this sample were examined simultaneously with 40 additional populations. This same outcome results for testing HWE after correction in the hypothetical population. However, the systematic deviation would be obvious by visual inspection of the uncorrected probabilities, a “vote-counting” approach. As noted by Chakraborty et al. (3), Bonferroni-type adjustments are warranted if researchers wish to minimize detection of false positives in genomic scans. More generally, controlling false discovery rate (9) has been advocated as a powerful approach for a variety of studies in this arena (10,11).

References


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