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## Comment on "Genetic Structure of Human Populations"

Rosenberg *et al.* (1) described the genetic structure of 52 human populations from five continents studied at 377 short tandem repeat (STR) loci. This high-resolution study demonstrated that, using multilocus information only, the individuals of these populations could be subdivided into five stable genetic clusters that correspond to five major geographic regions: sub-Saharan Africa, the Americas, Oceania, EastAsia, and Eurasia (Europe, the Middle East, Central and South Asia). The study also partitioned the total

among studies, we note that they did not base their analysis on the specific stepwise mutation model prevailing at STR loci, which is characterized by recurrent mutations. Ignoring the possibility that the same allelic type found in different individuals or populations may be derived from different evolutionary processes is known to lead to biased estimates of genetic structure (5–7).

By extracting information on the minimum number of mutations separating the alleles at all 377 loci (8), we reestimated (9)

A correct assessment of variability at the local or continental level is important not only for understanding the history of human settlement, but also for designing sound strategies to discover segments of our genome undergoing selection (10). Our analysis is in agreement with a previous study of minisatellite diversity showing that reduced variance components are obtained in the presence of high levels of homoplastic mutations (11). Our analysis also shows that this bias can be removed by using the right mutation model for STR loci, and suggests that the comparison of STR allele frequencies among different regions may be misleading. The demonstration that this huge data set is not flawed underscores its importance for estimating other important parameters of human population history.

**Table 1.** Past and present apportionments of human nuclear diversity.

Markers (ref.)	No. of loci	No. of population samples	No. of regions	Variability estimates (%) and 95% confidence intervals (12)		
				Between individuals within populations	Between populations within regions	Between regions
RFLPs (2)	79	11	5	84.5	3.9	11.7
STR (2)	30	14	5	84.5	5.5	10.0
Alu insertions (3)	21	32	5	82.9	8.2	8.9
STR (1)	377	52	5	93.2 (92.9, 93.5)	2.5 (2.4, 2.6)	4.3 (4.0, 4.7)
STR (1)	377	14	5	89.8 (89.3, 90.2)	5.0 (4.8, 5.3)	5.2 (4.7, 5.7)
STR, this study	377	52	5	87.6 (86.4, 88.9)	3.1 (3.0, 3.2)	9.2 (8.1, 10.4)
STR, this study	377	14	5	83.4 (81.2, 85.4)	5.1 (4.6, 5.7)	11.5 (10.0, 13.1)

genetic variance into components based upon differences between individuals within populations, between populations within regions, and between these five regions [table 1 in (1)]. Surprisingly, Rosenberg *et al.* (1) found very small differences between regions—only 4 to 5.7% of total diversity depending on regional sampling intensity, which is roughly half that of previous estimates inferred from molecular markers (2–4) (Table 1). Although the authors attributed that odd result to differences in sampling coverage

components of genetic variance under the same hierarchical structure as was used by Rosenberg *et al.* Our results (Table 1) differ significantly from those in (1) but are in perfect agreement with previous results obtained from other molecular markers with comparable sampling designs [with as much as 11.5% (95% CI: 10.0 to 13.1%) of total variability due to differences between regions, and only 83.4% (95% CI: 81.2 to 85.4%) due to differences between individuals within populations].

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### References and Notes

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8. The difference in the number of repeats between two alleles was inferred by taking into account the length of the motif of each STR, and the size of the amplified PCR fragments. STR alleles with imperfect motifs were discarded from the analysis.
9. The analysis of genetic structure was performed according to the model described in (5).
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12. Confidence intervals were computed from 20,000 bootstraps of the 377 loci.
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