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Correspondence

Small number of slowly-mutating (SM) Y-STRs not suitable for forensic and evolutionary applications

Dear Editor,

Recently in the Journal, Baeta et al. [1] reported on the development and validation of a multiplex tool for analyzing 6 Y-STRs that the authors selected from previously described markers [2] based on previously estimated mutation rates of $\sim 10^{-4}$ mutations/generation [3]. In this article, the authors advocated the use of these 6 slowly-mutating (SM) Y-STR markers, and their validated multiplex tool, in forensic and evolutionary studies. To our view, the advocated use of such small number of SM Y-STRs in forensic or evolutionary applications escapes any justification.

Although we generally agree that for certain evolutionary questions, Y-STRs with lower mutation rates may be more useful than those with higher rates, we regard it as unlikely that a small number of 6 such markers will provide evolutionary relevant information, questioning the advocated use in evolutionary studies. In principle, and in particular in the current days of evolutionary genetic studies being carried out with thousands of polymorphic DNA markers to avoid marker bias and to increase evolutionary relevant genetic information, and using SNPs rather than STRs [4,5].

More important for the Journal, we disagree with the authors' recommendation to use this small panel of 6 SM Y-STRs, and the multiplex tool they developed and validated, in forensic applications. As the authors reported in unrelated males from different population samples, gene diversity per marker (0–0.67) and haplotype diversity (0.70–0.95) are reduced, leading to low individual discrimination rates (22–62%). Although allele and haplotype differences between populations from different continental regions were highlighted, as expected when mutation rates decrease, these findings are typically not relevant for the proposed forensic application in kinship testing.

The authors particularly advocate the forensic use of these 6 SM Y-STRs and their multiplex tool "for confirming the exclusion in kinship cases where minimal discrepancies on one or a few loci are reported using regularly employed panels". Given the large number of unrelated males sharing the same 6 SM Y-STR alleles and haplotypes, as the authors reported, we cannot see how the use of these markers, and thus the multiplex tool, would benefit paternal kinship testing. There is a well-known direct relationship between Y-STR mutation rate and Y-STR diversity [2,3]. We regard it as naïve to expect the existence of a small set of Y-STRs with low mutation rates, as is appreciated in paternal kinship testing, that is polymorphic enough to allow differentiating between related and unrelated males in any efficient way, as is wanted with paternal kinship testing.

The authors argue that in paternal kinship testing where a discrepancy is observed at one or a few conventional Y-STRs "The assessment of additional disparities in the SM Y-STRs may provide further evidence for the genuine exclusion of the biological kinship, since mutation events are rarer to occur in these markers." However, in their reasoning, they seemingly ignored that it basically is the reduced mutation rate that leads to allele and haplotype sharing between related *and* unrelated individuals. Males with a nearly identical haplotype based on conventional Y-STR kits should always be considered as potential relatives in kinship testing. The probability of these 6 SM Y-STRs to differentiate males that nearly share a conventional Y-STR haplotype is very low, given their reduced diversity caused by their reduced mutation rates. Moreover, in contrast to a matching haplotype based on conventional Y-STRs, a matching haplotype based on these 6 SM Y-STRs does generally not allow differentiating between identity-by-state (IBS) and identity-by-descent (IBD), which, however, is the essence of paternal kinship testing.

As previously outlined in an article where the term slowly-mutating (SM) Y-STRs was first introduced [6], the number of SM Y-STRs needs to be large to perhaps become useful for paternal kinship testing, and certainly larger than that of conventional Y-STRs characterized by about 10 times higher mutation rates. The rationale behind this previously noted theoretical expectation is that only a large number of SM Y-STRs and their independent mutability may compensate for the low diversity per each marker caused by their reduced mutation rate. The same holds true for the use of SM Y-STRs in evolutionary studies. While a large number of Y-STRs with reduced mutation rates is available [3], empirical evidence for the suitability of SM Y-STRs to benefit forensic or evolutionary studies is yet to be presented.

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