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Allelic Association between the HUMF13A01 $(AAAG)_n$ STR Locus and a Nearby Two-Base Insertion/Deletion Polymorphic Marker

To the Editor:

We read with interest the paper of Hammond et al. (1994) published in a previous issue of the *Journal*. The authors present an extensive analysis of the distributions and frequencies of 13 microsatellite loci in four population groups, including Caucasians, Blacks, Mexican-Americans, and Asians. We would like to emphasize the promise of the method described for DNA typing in forensic use and medical applications and to give some additional molecular information on one of the short tandem repeat (STR) polymorphisms examined, the HUMF13A01 $(AAAG)_n$.

This locus is a tetranucleotide repeat that is highly polymorphic in all population groups examined so far (Polymeropoulos et al. 1991; Wall et al. 1993; Hammond et al. 1994). In addition to the alleles due to variable numbers of four-base repeats, Hammond et al. (1994) report the finding at relatively high frequencies of a variant allele, named "3.2", that does not correspond to a change in the number of reiterations of the core sequence. However, this allele is only described as "a fragment that migrates at the position of a fragment that is two bases longer than a fragment containing three repeats of the core sequence" (p. 186). No reference is made to the exact molecular nature of the 3.2 allele in the paper.

We have been analyzing the polymorphism of the HUMF13A01 STR locus by the PCR method of Polymeropoulos et al. (1991) in various human populations belonging to three major ethnic groups, Caucasians, Africans, and Asians. We have found in all groups the same variant allele as that reported by Hammond et al. (1994). Sequencing of PCR products of this allele in three individuals, one from each ethnic group, has shown that the variation does not affect the number of reiterations, but it is due to a two-base (GT) insertion/deletion polymorphism located just one base downstream of the repeated sequence (GenBank accession number M21986). In all ethnic groups, the deletion allele was always found in association with the four-repeat allele; on the other hand, the insertion was observed in association with a minority of the four-repeat alleles and with all the other alleles (table 1). These findings are fully consistent with the data of Hammond et al. (1994) and explain the molecular nature of the 3.2 allele. The distribution of the deletion/insertion polymorphism in Caucasians, Africans, and Asians suggests that the insertion allele is ancestral and that the deletion event occurred more recently on a four-repeat background, before the radiation of *Homo sapiens sapiens*. As a corollary, the complete association between the deletion and the four-repeat allele suggests that the HUMF13A01 STR alleles are mutationally stable and have most likely arisen only once during human evolution.

Table 1

Percent Frequencies of the GT Deletion/Insertion Alleles among HUMF13A01 STR Chromosomes Carrying or Not Carrying the $(AAAG)_4$ Allele

	F13A1 STR Chromosomes				
	Four-Repeat Alleles		Other Alleles		
Population	Del (3.2)	Ins	Del	Ins	No. of Chromosomes Tested
Caucasians[a]	12.3	2.8	.0	84.9	106
Africans[b]	12.0	7.0	.0	81.0	242
Asians[c]	23.0	16.2	.0	60.8	74

[a] 53 unrelated subjects from central Italy.
[b] 121 (50 Foulbe and 71 Mossi) unrelated subjects from Burkina Faso.
[c] 37 unrelated Chinese Li.

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