

Phenotypic Differences at the HUMvWA Locus Amplified with Different STR Kits

Sir:

The potential effect on the CODIS databanking program of a mutation in the primer binding site associated with an STR allele was recently encountered in our laboratories. A paternity analysis was performed in two laboratories using different STR kits. The original analysis was performed using a Profiler Plus kit from Perkin Elmer Biosystems (Foster City, CA) while the second lab performed testing for additional systems using the CTTV quadriplex and the Powerplex 1.2 kits available from Promega Corp. (Madison, WI). Additional testing was needed in this case to resolve the questioned paternity. The HUMvWA, D7S820, D13S317, and D5D818 loci were common to kits used in both laboratories and all loci except the HUMvWA system yielded identical phenotypes. The mother's phenotype differed for the HUMvWA locus depending upon the STR typing kit used. The Profiler Plus kit produced a homozygous HUMvWA phenotype for allele #17 whereas the CTTV quadriplex or the Powerplex 1.2 STR kits produced a heterozygous 17,18 phenotype (Fig. 1).

The most likely explanation for the discrepant phenotypes is that a single (or limited number) of nucleotides in the primer binding site(s) have been altered through mutation in the #18 allele in the mother's DNA template. Such a mutation could preclude the binding of one or both of the HUMvWA primers in the Profiler Plus kit to the #18 allele in the maternal template thereby resulting in a null allele.

Mutations associated with STR loci typically take the form of small additions or deletions of repeats from the parent allele pre-

sumably occurring during meiosis (1,2). More importantly here, null alleles have been observed for a number of STR systems with a mutation rate as high as 0.68% for the CYP19 system (2). A null allele in a parentage analysis can result in a false exclusion of an alleged father or mother when the overwhelming preponderance of other genetic evidence demonstrates the individual to be a true parent of a child. In such cases, statistical analysis of the data can incorporate the possibility of a mutation into the final probability of parenthood. In this particular case, the resulting paternity index calculated for the HUMvWA system was in error by a factor of two when using the Profiler Plus data because of the apparent homozygosity of the mother and its impact on the maternal transmission frequency for the #17 allele used in the calculations. Null alleles can have a more profound effect in forensic matching of an unknown assailant's STR phenotype with entries in a CODIS databank. For example, had the HUMvWA phenotype described here been produced in a crime laboratory using a Promega STR typing kit and then compared with entries in a CODIS databank containing the STR phenotype of the assailant produced using Profiler Plus, the results of the query at face value might be interpreted to exclude the CODIS entry as a possible contributor.

Null alleles have been reported for several of the 13 core loci included in the CODIS databanking program (HUMTPOX, D5S818, D16S539, HUMCSF1P0, and HUMTH01) (2). The HUMTPOX locus in particular exhibits a reported null allele rate of about 0.6% (2), which is similar to rates reported for more traditional mutations involving the addition or deletion of repeats from the tandem array. With a mutation rate of 0.6%, complications in CODIS matching due to mutations of the type reported here could be somewhat common occurrences. The CODIS matching program was developed in

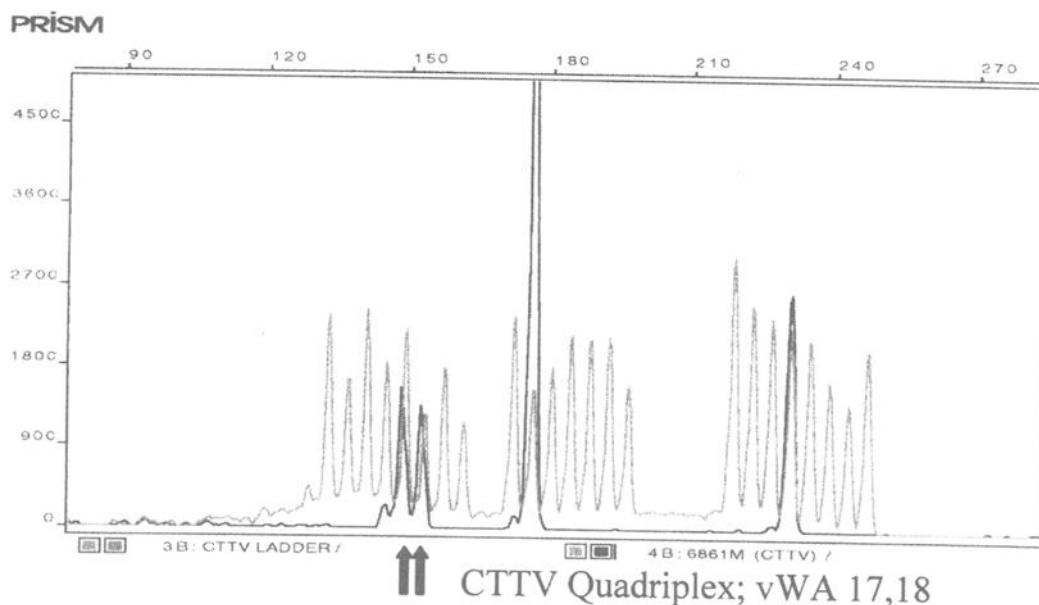


FIG. 1—Phenotypes for the HUMvWA locus in a sample amplified with STR kits from different manufacturers. A sample of DNA extracted from a buccal swab of the mother in a parentage analysis was subjected to STR typing using kits from Perkin-Elmer or Promega Corp. and the ABI 310 capillary electrophoresis system. The particular STR typing kit used to amplify the DNA and the HUMvWA phenotype are shown below each electropherogram along with vertical arrows denoting the positions of the HUMvWA alleles.

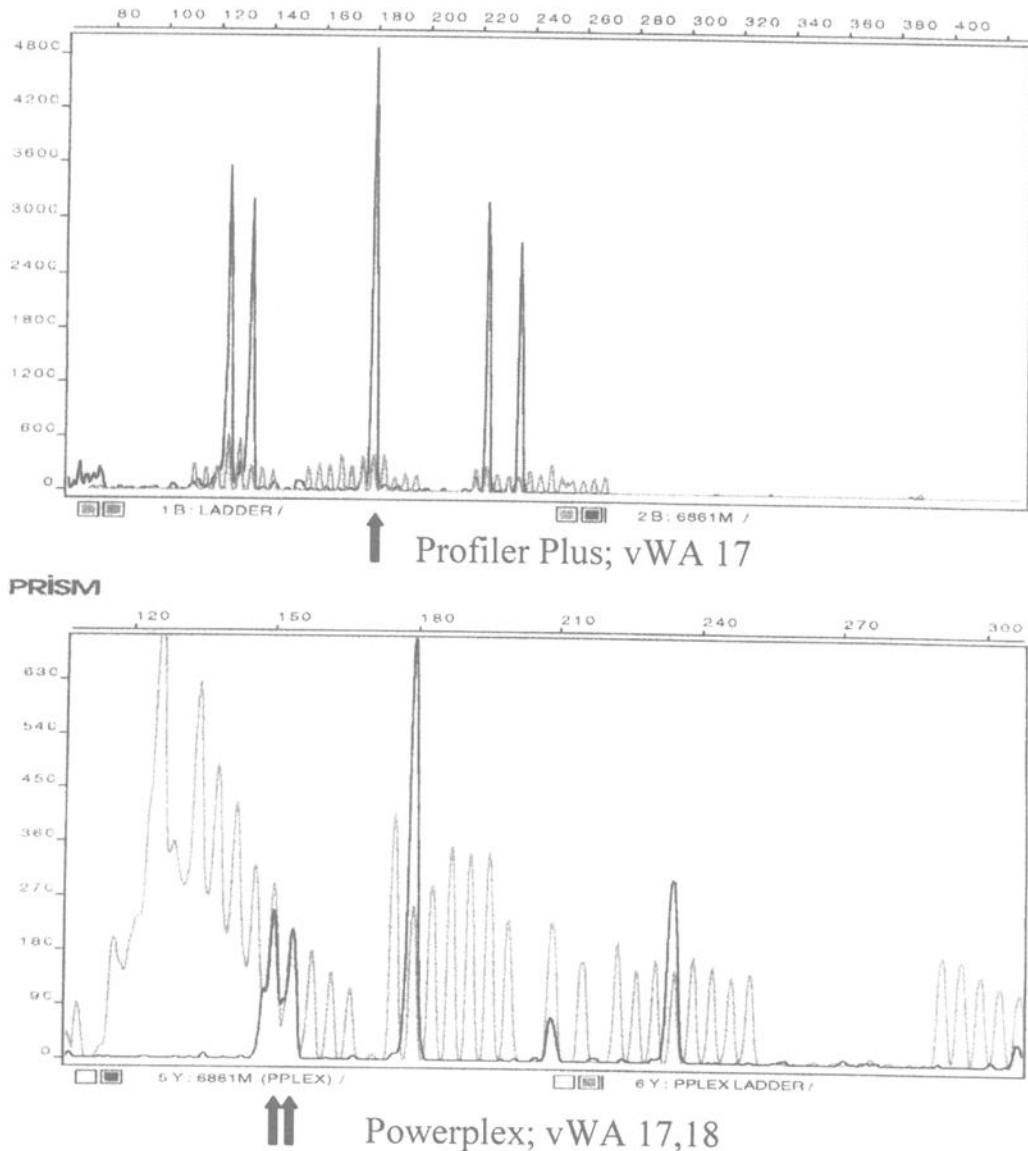


FIG. 1—(continued)

a manner that scores as positive “partial matches” between a query and database phenotype that differ for a limited number of alleles. Partial matches can result from errors in assigning a phenotype to a database entry or to a query phenotype. In addition, partial matches can result from a database entry and query that represent phenotypes from related individuals. As shown here, partial matches can also stem from mutations that produce null alleles when amplified using a particular STR typing kit. The key to identifying such mutations is the homozygous nature of one phenotype that matches one of the alleles in a heterozygous phenotype amplified from the same template with a different STR typing kit. When a partial match of this type is obtained, the crime laboratory may easily resolve the apparent discrepancy through repeat typing using an STR kit from a different manufacturer.

References

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2. Parentage Testing Standards Committee. Annual Report Summary for 1998. Bethesda, MD, American Association of Blood Banks.

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