B113 An Analysis of Unusual Mutation Patterns in Father-Son Pairs Using a ForenSeq™ DNA Signature Prep Kit and a YFiler™ Plus Polymerase Chain Reaction (PCR) Amplification Kit

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Learning Overview: The goal of this presentation is to present some unusual Y-chromosomal Short Tandem Repeat (Y-STR) mutations that led to discordance between a father and his sons.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by displaying examples of father-son discordance that, if not understood, could lead to wrongful convictions based on Y-chromosome analysis.

The application of Y-chromosome analysis is expanding in fields such as forensic science and genealogy. By researching the potential polymorphisms this chromosome can present, we can further our ability to assess DNA profiles for these disciplines to avoid erroneous exclusions of paternal linkage, wrongful convictions based on forensic evidence, and other misinformed genetic conclusions. The conservation of Y-haplotypes during transmission occurs due to lack of genetic recombination events in the inheritance of the Y-chromosome (with the exception of the pseudoautosomal region). However, mutation events can occur on the Y-chromosome, resulting in haplotype changes. These changes can include duplications and deletions that may occur at Short Tandem Repeat (STR) or Single Nucleotide Polymorphism (SNP) loci used in forensic DNA analysis. These mutation events can become important in cases of sexual assault where male-female mixture samples have low amounts of male DNA such that the male signal is not amplified in currently used STR multiplexes and analysis using Y-STR loci is used.

This study analyzed DNA from a father and his 11 sons using two different methods for forensic genetic analysis; next generation sequencing and capillary electrophoresis. The DNA from Council on Education for Public Health (CEPH) /Utah Pedigree 1413 was obtained from the Coriell Institute for Medical Research, Hamden, NJ, in the form of frozen DNA extracts isolated from a blood lymphocyte cultured cell line. Sample DNA was tested with the ForenSeq™ DNA Signature Prep Kit using primer set A and the YFiler™ Plus PCR Amplification Kit. Using these two platforms, three Y-STR loci were discordant between the father and each of his 11 sons. At all three loci, the father possessed the same allele as the sons, as well as one additional allele. At two of these loci (DYS449 and DYS635), the additional allele was one repeat (4 bp) longer than that of the shared allele. At the third locus (DYS458), the additional allele was three repeats (12bp) longer than that of the shared allele. Following read count and peak height analysis, it was concluded that these double allele loci did not result from the presence of a single true allele and a corresponding n-1 stutter allele. With the knowledge that the DNA was extracted from a blood lymphocyte cell line, it was postulated that a somatic mutation may be present in the cell line. However, this study was not able to determine whether the mutations exist in the blood of the father (therefore, true somatic mutations) or occurred as a result of the cell culture process.

Details concerning the position of these loci on the Y-chromosome, the repeat motifs of the alleles, and the potential for duplication versus stutter as the originating event will be discussed. Potential locus duplications were compared to those reported on the STRBase list of allele variations and to information found in literature. The observed DYS635 locus had an allele designation of 21, 22, which is reported on STRBase. The DYS449 and DYS458 loci showed potential allele-specific locus duplications that were not found on STRBase. The implications of non-inheritable allele patterns in the Y-chromosome, such as this, can be significant when considering comparisons between DNA obtained from germline cells (sperm) versus a known sample obtained from blood or saliva.

Y-Chromosome, Paternal Linkage, Locus Duplication

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