A134 Evolution and Molecular Basis of Microvariant Alleles of the D21S11 Locus

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The goal of this presentation is to examine the evolution and the molecular genetic basis of microvariant alleles of the D21S11 locus. Upon completion of this presentation, participants will have a better understanding of the complexity of the D21S11 repeat and its flanking regions, as well as the possible evolutionary development of the region.

This presentation will impact the forensic community because it offers a better understanding of the molecular basis of microvariant alleles and the evolution of D21S11 which is one of the most informative CODIS loci.

The CODIS locus D21S11 is a complex repeat that includes the presence of microvariants, or incomplete repeats, among certain alleles, typically those in the upper allele range. Microvariant alleles do not have a full length repeat and are therefore not an exact multiple of the original repeat pattern. These alleles are designated by the number of full repeats followed by a decimal point and number of bases in the partial unit. A complete repeat in D21S11 is a tetranucleotide, typically TCTA. The microvariant is a dinucleotide, usually presented as a TA immediately preceding the final repeat, and occasionally seen as a deletion of the TA found in the highly conserved middle section of the repeat structure. The incomplete repeat is thought to arise from single repeat gains and loses caused by replication slippage during DNA synthesis.

These microvariants are of unknown origin, but most likely arose individually by mechanistic processes (identity by state) or were fixed in an ancestral type and passed on by drift (identity by descent). The D21S11 repeat and flanking regions were sequenced in ten homozygous microvariant and non-microvariant human samples. An examination of the flanking regions of the alleles in all human samples revealed no polymorphisms, supporting the theory that the D21S11 structure is passed on through identity by descent. The internal structure of the microvariant alleles appears to have developed more recently via two separate events; one where the TA bases in the middle of the structure were lost and another where there was either an insertion of a TA immediately before the final repeat or deletion of a TC in the penultimate repeat. Although the finding had no impact on the ultimate results, complexities within the repeat region became apparent and only four of the samples were true homozygotes. The remaining six were motif heterozygotes at D21S11 but with the same overall number of bases in the repeat region.

In an attempt to understand the evolutionary process of D21S11 in humans, the repeat region was sequenced, and compared to a human reference, in four primate species: chimpanzee, gorilla, orangutan and siamang. Although the deeper molecular process is undoubtedly much more complex than what was observed in the limited number of primate sequences described here, notable polymorphisms were detected in both the flanking region and the repeat region. The analysis performed in the primate species confirmed evolutionary changes within the region. The current repeat structure at D21S11 is human specific as evidenced by mutations occurring after the evolutionary split of chimpanzee and human species. A final comparison of the human D21S11 reference sequence to the same region in a chimpanzee BLAST sequence provided a possible step-wise progression of evolution. The results of the comparison are consistent with a duplication within the repeat region of a common ancestor between human and chimpanzee that resulted in the current structure of the D21S11 locus in humans.

Due to the lack of polymorphisms in the flanking sequence among the human samples, there is no association between microvariants and a specific polymorphism in the regions contiguous to the repeat stretch of D21S11. Given this information, it is believed that the region is evolutionarily young. The D21S11 locus remains a strong genetic identifier.

Sequencing, D21S11, Microvariant

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