A158 Identification of Distant Relatives Using Haplotypes Constructed From Multiple Linked Autosomal STRs

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After attending this presentation, attendees will learn how linked autosomal STR loci can be used to support relationship in complex kinship cases. Additionally, attendees will learn how the presented genetic and statistical approaches can be applied to other complex kinship cases.

This presentation will impact the forensic science community by providing a new genetic approach to identify distant relatives when traditional forensic markers fail to provide sufficient statistical support for or against the hypothesized relationship.

Relatedness of living persons separated by multiple historical generations or by natural disaster or war can generally be determined if the survivors share a Y-chromosome haplotype or a mitochondrial DNA (mtDNA) sequence. However, establishing relatedness of individuals not expected to share Y or mtDNA sequences has posed a dilemma. This problem can be overcome by identifying haplotypes, each consisting of multiple closely linked autosomal STR markers, which are shared by the putative relatives but not present in large numbers of controls.

Remains of an American soldier missing since WWII were discovered in 2002 in Papua New Guinea. Mitochondrial DNA sequencing of his remains and of surviving maternal cousins led to his identification. The proposita, an Australian woman raised to believe she was the soldier's posthumous daughter, was not related to the soldier by mtDNA or Y lineages. Bones from the soldier's remains did not yield adequate DNA to genotype autosomal markers. Eight of the soldier's surviving relatives contributed DNA to compare with that of the proposita. Each of the eight relatives would be a second cousin of the proposita were she related to the family. Forty forensic STRs were genotyped in all persons using Identifiler™ and the NIST-developed 26plex, but these markers failed to provide sufficient statistical evidence for or against the hypothesized relationship. Therefore, clusters of linked STRs on each of multiple chromosomes were genotyped, and haplotypes were determined among undisputed relatives. On several chromosomes, genotypes of the proposita were consistent with haplotype sharing with one or more family members. To test whether these genotypes were shared by descent or by chance, 960 controls (1,920 chromosomes) with ancestry matched to the family were genotyped for the STRs in each linked cluster. It was critical to genotype multiple informative relatives so as to infer phase (haplotypes) of STR clusters to which unphased genotypes of the proposita could be compared. It was not necessary for the phase of genotypes among population controls to be known, so long as the presence of the index haplotype could be unambiguously excluded.

At several STR clusters, the proposita and her putative second cousins shared an entire haplotype not present among controls. For any one such cluster, the probability that the genotypes were shared by chance, rather than by descent, was less than 1/1920, or 0.00052 (upper 95% confidence limit, 0.00312). Based only on the upper confidence limit, the likelihood of the data is 320 times greater if the haplotypes belong to relatives of the proposita than if the haplotypes belong to individuals not related to her. The same reasoning holds for other STR clusters with haplotypes shared by the proposita and her putative second cousins and absent among controls. As many independent chromosomes

as necessary may be evaluated to provide additional statistical support for the test of relationship.

Identification of genetic relationship depends on individuals sharing genotypes by descent rather than simply by chance. Identity by descent can best be established when genotypes are very rare in the general population. Such rare genotypes can be defined by haplotypes constructed from linked markers.

Complex Kinship, Relatedness Testing, Linked Autosomal STRs

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