PATERNITY TESTING UTILIZING STR DNA ANALYSIS OF MALIGNANT TISSUE TO ESTABLISH THE IDENTITY OF A DECEASED MAN

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Following Mr. X. being charged with a historical sexual assault of his daughters, he was diagnosed with terminal lung cancer. Immediately following his death, prior to proper identification, his body was cremated. As a result of the circumstances surrounding the death, investigators had concerns with respect to the true identity of the deceased. In order to officially close the sexual assault case the investigators requested that DNA analysis be conducted to resolve the identity issue. Investigators were unable to locate any personal effects from Mr. X. with which to conduct a direct comparison. To ascertain whether Mr. X and the deceased were the same individual, a paternity analysis was attempted using a paraffin embedded lung biopsy sample believed to be from Mr. X, a sample from his biological daughter, and a sample from her biological mother.

DNA profiles were generated, utilizing the ABI STR Profiler Plus™ and COfiler™ systems, from two samples of the lung tissue and comparison blood samples obtained from the daughter (Daughter 1) of Mr. X as well as her biological mother (Ms. Y). The DNA profiles obtained from both samples of the paraffin embedded tissue were the same. The DNA profile from the biopsy sample was inconsistent with paternity at 3 of the 13 STR loci tested (D3S1358, D18S51, and D16S539) in relation to Daughter 1. Given the nature of the case, it was requested that a sample be submitted from an additional biological child (Daughter 2). In this case the biopsy sample profile was inconsistent with paternity at 1 STR locus (D18S51) only. At each of the inconsistent loci, the DNA profile from the biopsy sample appeared to be homozygous. The obligate paternal allele for both daughters at the D18S51 locus was a 14, while the biopsy sample profile appeared to be homozygous for the 17 allele.

Since DNA within malignant tissue is subject to an elevated rate of mutation, it is possible that these apparent inconsistencies are the result of somatic mutations in the biopsy sample. It is well documented that a loss of heterozygosity (LOH) occurs in numerous types of malignancies, including those involving the lung, and that they can be detected by microsatellite analysis. Part of the pathogenesis of cancer is believed to involve deletions in the area of tumor suppressor genes. Among the observed mutations in lung cancer, frequent allelic loss has been noted at the short arm of chromosome 3 (3p), in particular at 3p21 where the D3S1358 marker is located (Mitsuuchi et. al., Am J Med Genet. 2002 Oct 30;115(3):183-8. Review). Deletions or LOH have also been noted at 16q and 18q the general area of the STR loci D16S539 and D18S51 (Sato et. al., Genes Chromosomes Cancer. 1998 May;22(1):1-8 and Fong et. al., Cancer Res. 1995 Jan 15;55(2):220-3).

In light of the above it was concluded that the donor of the tissue (believed to be Mr. X) could not be excluded, at 12 STR loci, as the biological father of Daughter 2 (assuming that Ms. Y is her biological mother); and that an inconsistency was noted at one STR locus. Since the incorporation of germ-line mutation rates would not apply in this case, the Paternity Index was calculated using all loci except D18S51. It was also reported that no conclusive determination could be made with respect to the paternity of Daughter 1.

However, additional testing of these samples using the Promega PowerPlex® 16 system revealed a fourth inconsistency with paternity (Penta D) in relation to Daughter 1. The genotypes obtained in the different systems were the same at all loci (for the samples tested) reducing the likelihood of primer binding site mutations as an explanation for the observed inconsistencies.

To support the theory of LOH, thin sections of the paraffin embedded tissue were prepared and phenotypically different areas were isolated by Laser Microdissection using SL μCut equipment on loan from Molecular Machines & Industries. When typed in the PowerPlex® 16 system, one of these samples exhibited a 14 allele at the D18S51 locus confirming that the inconsistency observed at this locus can be explained by a LOH within the malignant tissue. These findings support the proposition that while malignant tissue is subject to a LOH, it may still be used to establish or reject familial association.