G9 Cancer Patient mtDNA Forensic Identification: A Case Report

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After attending this presentation, attendees will understand how to manage a forensic identification case in a cancer patient, when only neoplastic tissue is available for the genetic analyses.

This presentation will impact the forensic science community by demonstrating that, because of the frequency of mutations in mtDNA is higher than in nuclear DNA in a variety of human cancers (as suggested from several studies), the mtDNA profiling should not be applied as the unique analysis in cases of forensic identification of cancer patients when only neoplastic tissue is available. Moreover, direct automated sequencing lacks adequate resolution to detect mtDNA heteroplasmy when, as in cancer cells, the somatic mutation tend to homoplasmy.

Mitochondrial genome mutations are described in many kinds of human malignancies, including lung cancer. These mutations can be base substitutions, insertion, or deletions, and the 1.1 kb d-loop region has been recently identified as a mutational "hot spot" in the mitochondrial DNA (mtDNA) of neoplastic tissue. Cancer cells harbor homoplasmic rather than heteroplasmic mutations; therefore, somatic mutant mtDNA appears as a single copy among a majority of wild-type mtDNA molecules and becomes dominant in the cancer cell probably due to the growth/survival advantages that such mutation confers to the cell.

A case of forensic identification will be presented in which a widow claimed medical malpractice by the physicians that had taken care of her husband, who was affected by a malignant lung disease. The wife thought that he had been wrongly diagnosed with cancer and, therefore, he had undergone massive and inappropriate therapies that finally led him to death.

In this case, the prosecutor ordered the seizure of the neoplastic histological samples attributed to the deceased and the comparison of the genetic profile obtained from these samples with those of the relatives, in order to establish the presence or absence of genetic compatibility among the neoplastic tissue and the relatives of the deceased.

To this end, autosomal markers were analyzed and compared with those of the two daughters of the deceased, while Y-chromosome markers and mtDNA were analyzed and compared with those of his brother.

While both autosomal and Y-chromosome markers confirmed the correspondence of the histological samples to the deceased, in the case of mtDNA a difference at nucleotide 16093 of HVRI region has been highlighted: in fact the brother had a C while the lung tissue examined showed a transition from C to T. In order to ascertain the full genetic compatibility it was therefore necessary to study the nature of this nucleotide difference by cloning of PCR products.

Sequencing of PCR cloning products thus allowed highlighting a heteroplasmic site (tending to homoplasmy) at nt.16093 in tumor cells with respectively 75% of mutated mtDNA and only 25% of germ-line mtDNA compatible with the brother reference sequence.

mtDNA Profiling, Heteroplasmy, Neoplastic Tissue

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