B166 Loss of Heterozygosity at Several Loci of the 13 CODIS Core STR Loci in a Patient Diagnosed With Cancer

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After attending this presentation, attendees will have an increased awareness of the possibility of a complete or partial loss of heterozygosity in a single source sample at multiple locations in nuclear DNA as a result of deletions due to cancer.

This presentation will impact the forensic community and/or humanity by making scientists aware of the possibility of observing a loss of heterozygosity in a single source sample, which may be misidentified as a mixture when an inadequate number of loci are tested.

It has been documented that a loss of heterozygosity in one of the systems of the 13 CODIS core STR loci can occur due to actual autosomal rearrangements associated with cancer. It is also known that a loss of heterozygosity can be observed in poor quality DNA samples from paraffin embedded tissues resulting in stochastic effects during amplification. In this particular case, a loss of heterozygosity was seen at more than one locus in several specimens with some specimens exhibiting a loss of heterozygosity at up to four loci.

After a patient's untimely demise from cancer, slides used in the patient's diagnosis were submitted for DNA analysis via STR testing to ensure that the tissue on the slides was not contaminated by another patient's tissue during the preparation process for evaluation by a pathologist. The patient in this case had initially been diagnosed with nonHodgkin's Lymphoma. After treatment with chemotherapy, the lymphoma was declared to be in remission. Approximately one year later, the patient was found to have a growth in one of his lungs. This tumor was subsequently diagnosed as being small cell carcinoma also known as oat cell carcinoma. While being treated for the lung tumor, the patient suffered a relapse of the non-Hodgkin's Lymphoma. Although it was noted that the lung tumor had begun to decrease in size the patient passed away a short time later. Upon autopsy, there was no indication of the lung tumor and the involved parties sent the paraffin blocks and related slides used to diagnose the small cell carcinoma to two private forensic DNA laboratories in order to determine the possibility of specimen mis-handling.

Peak imbalances observed in the samples tested from the patient led the first forensics laboratory performing testing to conclude that the samples were a mixture of the patient and another individual. However, none of the eight loci tested exhibited more than two alleles.

The second laboratory (Orchid Cellmark Dallas) then received three paraffin blocks and nine corresponding slides for testing and comparison with STR testing. Portions of the paraffin blocks and related slides were subjected to organic extraction via phenol chloroform and extracts were purified and concentrated using Microcon® centrifugal filter units. The extracts were quantitated and initially amplified using Applied Biosytem's Profiler Plus® Kit. At a later date, the samples were also amplified using Applied Biosystem's Cofiler® Kit.

After injection into Applied Biosystem's 310 Genetic Analyzer®, analysis was performed using Applied Biosysem's GeneScan® and Genotyper®. This analysis revealed severe peak imbalances in several specimens at D3S1358 (in both Profiler Plus® and Cofiler®), Amelogenin (in both Profiler Plus® and Cofiler®), D8S1179, D21S11, D5S818, D13S317, D7S820 (in Profiler Plus® only) and actual complete loss of heterozygosity at D5S818 and D13S317 in two samples. As seen in the data, the loss of heterozygosity was neither more prevalent in the smaller systems nor the larger systems. The peak imbalances varied from sample to sample inasmuch as there were not only differences in the percentages of peak RFU's, there were also discrepancies as to which systems revealed peak imbalances. Throughout all thirteen loci, no more than two alleles were observed.

Several months later, tissue slides prepared at autopsy were received and tested using methods identical to those used for the lung tissue slides. Although the autopsy slide tissue seemed to be more degraded than the lung tissue slides, the results obtained showed the same peak imbalances consistent with a loss of heterozygosity.

Heterozygosity, STR, Cancer

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