H137 Next Generation Sequencing Technology for the Identification of Genetic Markers Associated With Sudden Unexplained Death and Sudden Infant Death Syndrome

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After attending this presentation, attendees will understand how the use of next generation sequencing technology to identify genetic markers associated with Sudden Unexplained Deaths (SUDs) and Sudden Infant Death Syndrome (SIDS) can provide a lower-cost alternative to traditional genetic testing methods.

This presentation will impact the forensic science community by demonstrating the potential advantages of using next generation sequencing to identify genetic markers associated with SUDs and SIDS and the advantages of this approach over existing methods.

In the United States each year, there are thousands of deaths of young adults and infants for which there is no determinable cause of death at autopsy. After postmortem investigation, these cases are often listed as SUDs or SIDS. It is estimated that up to 30% of SUD and 10% of SIDS cases could be attributed to potentially lethal and heritable mutations in genes associated with cardiac function. Tests are currently available to identify these genetic variants; however, due to the labor-intensive nature of the traditional sequencing methods used, the identification of putative SIDS/SUD mutations can cost $5,000 or more per case to sequence only 11 of these genes. This type of testing is prohibitively expensive for medical examiner's and coroner's offices. The purpose of this project was to develop and validate a cost-effective molecular autopsy tool to aid in the determination of cause of death for autopsy negative SUD and SIDS cases. In collaboration with the Baylor College of Medicine Human Genome Sequencing Center, the exomic regions of 65 genes implicated in cardiac arrhythmia and/or sudden death were sequenced using next generation sequencing on the Illumina® HiSeq platform. This allowed a sequencing of a much greater number of genes with a ten-fold *decrease* in cost. More than 300 decedent samples from a Harris County Institute of Forensic Sciences SIDS and SUD cohort were sequenced for lethal mutations. Within this cohort, over 1,000 potential pathogenic variants were identified. After a comprehensive biochemical and functional analysis, the cases where pathogenic mutations were identified were further analyzed for confirmation by the Baylor College of Medicine Medical Genetics Laboratory, a Clinical Laboratory Improvement Amendments (CLIA) -accredited laboratory. Approximately 3%-5% of the cohort was identified as having a lethal genetic mutation, which is significantly less than previously reported estimations. Studies in collaboration with Baylor College of Medicine Center for Medical Ethics and Health Policy are ongoing to develop criteria for reporting final results to family. This presentation will summarize the methods and the sequencing results as well as the process for confirming the findings and proposed reporting guidelines.

Next Generation Sequencing, SIDS, SUDS