NEXT GENERATION SEQUENCING TECHNOLOGY FOR THE IDENTIFICATION GENETIC MARKERS ASSOCIATED WITH SUDDEN UNEXPLAINED DEATH AND SUDDEN INFANT DEATH SYNDROME

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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 post-mortem investigation, these cases are often listed as Sudden Unexplained Death (SUD) or Sudden Infant Death Syndrome (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 $15,000 or more per case to sequence only eleven 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 sixty five genes implicated in cardiac arrhythmia and/or sudden death were sequenced using next generation sequencing on the Ilumina HiSeq platform. This allowed us to sequence a much greater number of genes with a five-fold *decrease* in cost. Over four hundred decedent samples from a Harris County Institute of Forensic Sciences SIDS and SUD cohort were sequenced for potentially lethal mutations. Within this cohort, the cases where pathogenic mutations were identified were further analyzed for confirmation by the Baylor College of Medicine Medical Genetics Laboratory, a CLIA accredited laboratory. 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.