H120 Thanatotranscriptome: Gene Expression in Cadaver Livers

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After attending this presentation, attendees will understand how to use the thanatotranscriptome to gain further insight into the pathways involved in the apoptotic machinery after death. Specifically, attendees will learn that RNA is stable in liver tissue of cadavers, and it is a suitable molecule for profiling gene expression even at longer periods of time after death up to 48 hours.

This presentation will impact the forensic science community by informing practitioners interested in using postmortem apoptosis patterns of select cadaver tissues with the goal of providing a method to estimate Postmortem Interval (PMI).

Gene expression investigations are a well-established part of antemortem studies with broad arrays of applications. Unfortunately, the study and implementation in the forensic fields are still in their infancy. The study of thanatotranscriptome apoptotic genes may prove useful relative to providing molecular evidence of active life after death. The goals of the study are to provide detailed insight into expression of 84 key genes involved in complex apoptotic pathways from liver tissues from actual, whole cadavers autopsied in forensic cases.

Tissue samples were removed by a medical examiner from the livers of four non-sequential victims of a heart attack caused by coronary heart disease and gunshot wounds. Complementary DNA (cDNA) was synthesized and the concentration was measured. To investigate the relationship between PMI and the expression levels of apoptosis, quantitative Polymerase Chain Reaction (PCR) arrays for specific apoptotic genes were performed. The PCR array contained the following five functional gene groups: (1) anti-apoptosis; (2) caspases and regulators; (3) death domain proteins; (4) induction apoptosis; and, (5) regulation of apoptosis. The apoptosis-related gene expression profile was assessed using human PCR arrays. The results show substantial down-regulation of the expression of anti-apoptotic functional gene groups when liver tissues from the control cadaver were compared with cases of increasing time of death. Significant anti-apoptotic genes such as *BAG3*, *BAK1*, *BAX*, *BIRC5*, *IL10*, *NAIP*, *NFKB1*, and *RIPK2* demonstrated expression reduced more than six-fold; however, gene expression levels of negative regulators of apoptosis such as *BCL10*, *BCL2L2*, *BCL2*, *CD40LG*, and *CIDEA* were also reduced. Additionally, the expression of death domain proteins such as *TNFRSF10A*, *TNFRSF11B*, *YNFRSF25*, *TNFRSF9*, and *TNFRSAF* was down-regulated more than three-fold. Certain genes responsible for the induction and positive regulation of apoptosis were greatly overexpressed. *ABL1*, *AIFM1*, *CIDEB*, *PYCARD*, and *TNFRSF10B* gene expressions increased greater than two-fold. *Caspases* and their regulators such as *CASP3*, *CASP4*, and *CASP9* gene expressions were also considerably up-regulated; however, the expression of the anti-apoptotic gene *XIAP* was also greater than 28-fold overexpressed.

This study was an analysis of the yield and apoptosis gene expression after a host dies as the interval of time since death increased in liver tissues of forensic cases. The results of this study demonstrate that optimum RNA extraction yields can be obtained even at a PMI of 48 hours. This result also suggests that RNA stability is viable for gene expression analysis from liver sample of cadaver cases.

In conclusion, this study shows RNA stability in liver postmortem samples, which makes it a suitable molecule for gene expression studies even at longer periods of time lapse up to 48 hours after death. The study design demonstrates a technique that will meet the demand for rapid and reproducible thanatotranscriptomic methods to correlate apoptotic gene expression patterns to establish a possible biomarker for estimating PMI.

Cadaver, RNA, Thanatotranscriptome

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