OSAC RESEARCH NEEDS ASSESSMENT FORM

Title of research need: Understanding the Genetic Risks of Sudden Death

Keyword(s): Unexplained Sudden Death, Seizure, Arrythmia

Submitting subcommittee(s): MDI **Date Approved:** 6/30/2025

Background Information:

1. Does this research need address a gap(s) in a current or planned standard? (ex.: Field identification system for on scene opioid detection and confirmation)

No.

2. Are you aware of any ongoing research that may address this research need that has not yet been published (e.g., research presented in conference proceedings, studies that you or a colleague have participated in but have yet to be published)?

No.

3. Key bibliographic references relating to this research need: (ex.: Toll, L., Standifer, K. M., Massotte, D., eds. (2019). Current Topics in Opioid Research. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-88963-180-3)

Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2018 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/ucd-icd10.html on Mar 11, 2020 5:36:08 PM

Michael Ackerman, Dianne L Atkins, John K Triedman, Sudden cardiac death in the young Circulation. 2016 Mar 8; 133(10): 1006–1026. doi: 10.1161/CIRCULATIONAHA.115.020254 PMCID: PMC5033115

Nupoor Narula, David J. Tester, Anna Paulmichl, Joseph J. Maleszewski, Michael J. Ackerman, Post-Mortem Whole Exome Sequencing with Gene-Specific Analysis for Autopsy Negative Sudden Unexplained Death in the Young: A Case Series, Pediatr Cardiol. 2015 Apr; 36(4): 768–778. Published online 2014 Dec 13. doi: 10.1007/s00246-014-1082-4 PMCID: PMC4907366

Lin Y, Gryazeva T, Wang D, Zhou B, Um SY, Eng LS, Ruiter K, Rojas L, Williams N, Sampson BA, Tang Y. Using postmortem formalin fixed paraffin-embedded tissues for molecular testing of sudden cardiac death: A cautionary tale of utility and limitations. Forensic Sci Int. 2020 Jan 30;308:110177. doi: 10.1016/j.forsciint.2020.110177. [Epub ahead of print] PMID: 32155531

4. Review the annual operational/research needs published by the National Institute of Justice (NIJ) at https://nij.ojp.gov/topics/articles/forensic-science-research-and-development-technology-working-group-operational#latest? Is your research need identified by NIJ?

No.

5. In what ways would the research results improve current laboratory capabilities?

The U.S. medicolegal death investigation (MDI) system is charged with investigating all sudden and unexpected causes of death. In 2018, however, CDC Wonder reported 5,711 individuals under 50 years of age died without a cause of death identified.1 Understanding genetic factors that lead to sudden death are hampered by the cost of genetic analysis and the evolving science that surrounds it. Specific recommendations for the utilization of genetic testing in MDI investigations of sudden death are also unstandardized and evolving. As costs are decreasing, the availability of choices for genetic testing have increased. Some examples include, but are not limited to, targeted sequencing panels, whole exome sequencing, and whole genome sequencing. Targeted Sequencing Panels (TSP) test for a select number of specific genes or coding regions within genes that are known to harbor mutations that contribute to disease and may include information that will guide a clinician's plan of care and it is conceivable that this kind of testing could apply to the postmortem setting as well. Whole Exome Sequencing (WES) allows variations in the protein-coding region of any gene to be identified, rather than in only a select few genes. Because most known mutations that cause disease occur in exons, whole-exome sequencing is thought to be an efficient method to identify possible disease-causing mutations. However, exomes make up only about 2% of the whole genome and of the 20,000 genes on the exome, approximately only one-third is well understood. Whole Genome Sequencing (WGS) determines the order of all the nucleotides in the entire genome and can determine variations in any part of that genome. What is the role of genetic testing in this publicly mandated death investigation system? What is the role of the public health system in this regard? And what are the rights of the surviving family members whose health risk may rely on the accurate cause of death of their loved one? The medicolegal death investigation system needs research to better understand and recommend the utility of specific genetic analysis in investigating sudden death, as well as prioritization of samples routinely
stored for this purpose.

6. In what ways would the research results improve understanding of the scientific basis for the subcommittee(s)?

Research to improve our understanding of genetic risk factors associated with sudden death would allow for more accurate causes of death and the improved identification and medical care of family members at risk.

7. In what ways would the research results improve services to the criminal justice system?

Our improved understanding of our genome and related genetic analysis in MDI would allow the criminal justice system to appropriately demonstrate the risk of disease versus alternate cause of death of an individual.

8. Status assessment (I, II, III, or IV): II

	Major gap in current knowledge	Minor gap in current knowledge
No or limited current research is being conducted	I	III
Existing current research is being conducted	II	IV

This research need has been identified by one or more subcommittees of OSAC and is being provided as an informational resource to the community.