Copy number variant detection in post-mortem samples

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Forensic molecular autopsies can be used as a complement to standard medical autopsies to deduce a potential genetic cause of a sudden unexplained death. At the National Board of Forensic Medicine in Sweden, roughly 80-100 cases each year are analyzed using a targeted gene panel focusing on sudden death. However, current methods allow only the detection of small variants, e.g. SNVs, and indels up to perhaps 10-20 bps. A study by Mates et al. 2020 (https://doi.org/10.1016/j.fsigen.2020.102281) suggested that roughly 10-15% of unexplained deaths could have a genetic copy number variant (CNV) leading to sudden cardiac death.

In the current study, we explore the potential of CNV detection in our targeted gene panel consisting of a total of 2422 genes with relevance to sudden death. We prepare sequencing libraries for a total of 100 post-mortem samples and enrich using a highly uniform hybridization capture approach and finally sequence the enriched libraries on an Illumina NextSeq 550. In addition, a subset of samples are analyzed using PCR-free whole genome sequencing.

We use a plethora of different bioinformatic methods suitable for targeted exon data to find CNVs. The results suggest that post-mortem data needs pre-processing prior to CNV analysis due to the heterogeneity of quality and quantity of input DNA and further that not all samples are suited for CNV detection. The study will further present clinically relevant findings in the data.