Low Copy Number (LCN) DNA

DNA scientists, particularly those involved in anthropology or forensics, are often faced with the challenge of trying to analyze samples that have less than 100 picograms of DNA. In response to this need, scientists have developed modified methods that have successfully analyzed the miniscule amounts of DNA left behind on a single fingerprint, a single human hair (without the root), from laundered clothing, and even from saliva left in a bite on a body that was submerged for several hours, to list only a few examples[3,4,5]. Referred to as trace DNA or low copy number (LCN) DNA, these powerful techniques only require the DNA from a few cells. To give you an idea of how sensitive these techniques are; a penny weighs around 3 grams, whereas a typical human cell has about 3 picograms of DNA. So a penny weighs about the same as a million cells and we only need two to ten cells to analyze using trace DNA methods.

But LCN or trace DNA analysis comes with a price a much higher chance of obtaining artifacts. Premier among the problems encountered with trace DNA analysis is contamination. DNA contamination can occur from a number of sources:

1. Extraneous DNA at the collection site: extraneous DNA can occur due to natural mixtures that may occur such as blood, other bodily fluids or even just sloughed skin cells from the victim or from other occupants, just by happenstance;
2. Unintentional contamination from investigators at the site; or
3. Contamination in the laboratory.

Even with appropriate controls, mixed DNA profiles are often encountered and it is necessary to eliminate all possible sources of DNA. To this end, it is advantageous to obtain DNA samples from as many potential contributors as possible such as other occupants, investigators and laboratory personnel, for comparative analysis and elimination from the profile.

Even without contamination issues, a number of other anomalies can plague trace DNA analysis[2]. For instance, in the short tandem repeat (STR) analysis commonly employed in forensics and paternity testing, these include:

- Allelic dropout: Due to preferential replication of some alleles over others including shorter ones over longer ones, certain alleles may not be replicated sufficiently for detection. Often it is difficult to tell if there is allelic dropout or if the allele is homozygous.
- Stutter peaks, which commonly occurs about one repeat away from the real peak, may be higher than usual and selectively called by the software, referred to as false alleles.
- Additional allelic peaks: Incomplete and preferential replication, as with allelic dropout, can cause additional spurious peaks.
- Recent evidence suggests that the Taq polymerase loses fidelity during the extended reactions required for trace DNA analysis, resulting in G to C transitions and erroneous allele calls[1].

Yet, even given all the limitations and possibilities for anomalies, the necessity for trace DNA analysis will continue to increase as it is often the only method available for analyzing ancient DNA specimens or to solve a heinous crime. Therefore it is imperative that DNA scientists working in this arena are thoroughly familiar with the strengths and weaknesses of the technique and methods to overcome those limitations.

References:

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