SNP RECOVERY FROM DEGRADED SAMPLES FOR KINSHIP ASSESSMENT

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The Armed Forces Medical Examiner System's Armed Forces DNA Identification Laboratory (AFMES-AFDIL) is charged with assisting the Defense POW/MIA Accounting Agency (DPAA) in providing the fullest possible accounting of missing US service members from prior conflicts. The AFMES-AFDIL extracts and analyzes DNA from DPAA submitted samples and compares the genotypic results to family reference specimens (FRSs) to determine whether they are related. DNA from these bone samples is highly degraded due to time, deposition condition, fire, and/or preservation methods. When maternal relatives are available, mtDNA analysis can be used to compare samples, but when such relatives are unavailable, or the service member has a common haplotype, additional testing is required to determine identity. Parabon NanoLabs developed a novel method for detecting kinship (out to 6th-degree relatives) using 100,000 or more autosomal SNPs. Like mtDNA, SNP data can be generated from samples too degraded for STR testing, and SNP analysis also opens a wider pool of potential family reference donors, regardless of the relationship type. While AFMES-AFDIL has pioneered a number of approaches for obtaining DNA data from extremely challenging samples, the possibility of generating sufficient numbers of autosomal SNP genotypes to support Parabon's kinship model needed to be explored. This joint project between AFMES-AFDIL and Parabon closed the gap between the number of SNPs that can be attained from highly degraded DNA samples and the minimum number of SNPs needed for accurate kinship prediction.

Given AFMES-AFDIL's success in using hybridization capture for targeted enrichment of human DNA sequences from degraded case samples, a SNP capture kit was designed to target genome-wide SNPs for downstream sequencing and data analysis. A set of 15,000 SNPs that offered the highest resolution of 3rd and 4th degree relatives was selected by Parabon for inclusion. The kit was tested on five World War II, Korea, and Vietnam non-probative bone samples, and the SNP genotypes were compared in the blind to a panel of FRSs. Despite significant allele dropout, as expected from degraded DNA, Parabon's kinship algorithm was able to successfully identify the correct FRS for each sample and detect a distant relationship between two FRSs, with low false positive rates. This presentation will show how hybridization capture can be used to generate accurate SNP genotypes from extremely degraded samples, and how autosomal SNP analysis can be used for efficient detection of distant kinship relationships.