B5 An Evaluation of a Novel Massively Parallel Sequencing (MPS) 74-Microhaplotype Panel for Biogeographic Ancestry Prediction

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After attending this presentation, attendees will understand the potential of using novel Microhaplotype (MH) markers in addition to Single Nucleotide Polymorphism (SNP) panels for predicting the biogeographic ancestry of individuals.

This presentation will impact the forensic science community by illustrating the usefulness of an MPS MH panel to enhance the prediction of individuals' ancestry and to extrapolate valuable information on the minor contributor's profile in mixed DNA samples.

MHs are loci of two or more SNPs within a short distance of each other (<300 nucleotides) with three or more allelic combinations. The standard Sanger sequencing method does not enable determining the cis/trans relationship between SNP alleles within the same amplicon (i.e., haplotype) whereas MPS methods, which allow specific clonal sequencing of each individual DNA strand, can distinguish the parental haplotypes at a given locus. The key features of MH markers, such as small amplicon size, multi-allelic nature, absence of stutter peaks, and lower mutation rate than conventional autosomal and sexual linked Short Tandem Repeats (STRs), also make them an additional candidate marker for forensic identification, mixture deconvolution, and ancestry prediction purposes.[1] The most common method for ancestry prediction utilized is based on SNPs, which are of little use in mixtures given their bi-allelic nature. The goal of this project was to evaluate whether MPS-based MH analysis could be effective in the prediction of the biogeographic ancestry of individuals in cases of mixed samples where the use of SNPs is more challenging.

A set of 91 European-Americans (EAs), 54 African Americans (AAs), 87 Hispanics (HISs), and 51 Native Americans (NAs) was selected and analyzed on the Ion Chef/Ion S5™ MPS platform using a 74 MH panel specifically developed for improving the accuracy of ancestry prediction. To calculate the Random Match Probability (RMP) of each MH profile from the specific population of interest, allele frequencies from numerous populations, previously inferred with PHASE software, were used.[2] In particular, the RMP calculated for the full population sample sets was observed to be higher in all populations in which individuals self-identified as such. In addition, Likelihood Ratio (LR) values were calculated by dividing the highest RMP obtained among the four populations by the second highest. The resulting LR value expresses how much more likely it is to observe the given profile if it originated from an individual belonging to the population at the numerator than if it originated from an individual belonging to the population at the denominator. The biogeographic ancestry of representative EA, AA, HIS, and NA population samples was correctly predicted and the related LR values were found to be at their highest in the corresponding population of origin. These results support the hypothesis that the novel MPS 74 MH panel is a useful forensic assay that enables effective biogeographic ancestry prediction complementing the accuracy of current binary and non-binary marker-based ancestry prediction tools.

Reference(s):

1. Pakstis AJ, Fang R, Furtado MR, Kidd JR, Kidd KK. Mini-haplotypes as lineage informative SNPs and ancestry inference SNPs. *European Journal of Human Genetics*. (2012) 20(11): 1148-1154.

2. Kidd KK, Speed WC, Pakstis AJ, Podini DS, Lagacé R, Chang J, Wootton S, Haigh E, Soundararajan U. Evaluating 130 microhaplotypes across a global set of 83 populations. *Forensic Science International: Genetics.* (2017) 29:29-37.

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