A89 A Custom Bioinformatics Tool to Detect Amelogenin Y Allele Dropout in Males

Jessica Saunier, BS, Armed Forces DNA Identification Laboratory, 1413 Research Boulevard, Rockville, MD 20850; and Michael D. Coble, PhD, Armed Forces DNA Identification Laboratory, 1413 Research Boulevard, Building 101, 2nd Floor, Rockville, MD 20850*

The goal of this presentation is to describe the frequency of Y- dropout in a global population database of 1572 samples and to provide a method for the identification of samples with potential Y - dropout. How this process was utilized by the Armed Forces DNA Identification Laboratory (AFDIL) to detect samples and determine the frequency of Y- dropout in its population databases will be demonstrated.

This presentation will impact the forensic community by teaching how to detect samples with potential Y-dropout using a customized macro developed at AFDIL, and will understand the forensic implications of Y-dropout.

Amelogenin is a single copy gene with homologs on the X (AMGX) and Y (AMGY) chromosomes, and is commonly incorporated in commercially available short tandem repeat (STR) kit for human sex identification in DNA databasing and forensic casework. The most commonly used amelogenin primer sets target a region of the first amelogenin intron containing a six base pair (bp) deletion among the AMGX and AMGY alleles.[1] Amplification of both the X (106 bp) and Y (112 bp) alleles indicate a male genotype, while the presence of a single X (106 bp) allele indicates a female genotype. The absence of the 106 bp X-allele does not interfere with gender identification if the 112 Y-allele is present, as the Y-allele indicates the presence of the Y-chromosome.[2] However, absence of the Y-allele, due to mutations and/or deletions in the Y-derived fragment of the amelogenin gene that create an amplification failure, could potentially result in a mistyping of the correct sex.

Frequent Y-dropout has been observed in similar ancestor lineages and in distinct regions of the world, particularly among populations native to the Indian subcontinent [3]. The AFDIL Research Section has previously databased 1572 profiles from Western, Southern, and Central Asian populations using the PowerPlex® 16 System (Promega, Madison, WI). Given the increased frequency of Y-dropout in some of these regional populations, we have investigated the frequency of Y-dropout within our global population databases and have developed a process for the identification of samples with potential Y-dropout.

In order to detect Y-dropout among samples processed in an otherwise streamlined procedure (using electronic data transfer between data reviews and LIMS storage) we have developed a custom macro to flag samples that may have Y-dropout. The macro automatically reads GeneMapper export files and identifies samples with peak imbalance at amelogenin based on the ratio of homozygote and heterozygote RFUs across the entire profile.

The custom designed macro was tested on all 1,572 population samples, and on control samples consisting of known females and males with known Y-dropout. Samples flagged by the macro were subjected to a series of confirmatory tests. All samples were typed with a X- chromosomal STR multiplex which includes SRY, the male sex- determining gene located on the Y-chromosome. In addition, samples were also typed using the AmpFlSTER® Yfiler™ (Applied Biosystems, Foster City, CA) kit which amplifies Y-chromosomal DNA.

Obtaining the frequency of Y-dropout can be important when databasing a large number of samples, particularly when samples are from regions of the world where Y-dropout in the course of standard sample typing occurs more frequently. We will report on the results of our study among 1572 profiles from Western, Southern, and Central Asian populations and discuss this new tool as a method for the identification of Y-dropout.

The opinions and assertions contained herein are solely those of the authors and are not to be construed as official or as views of the United States Department of Defense or the United States Department of the Army.

References:

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Amelogenin, Y-Dropout, Y-Chromosome

 ** Presenting Author*