PROTEOMIC GENOTYPING: USING MASS SPECTROMETRY OF HAIR PROTEIN TO INFER SNP GENOTYPES

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Proteins are an intrinsic part of biological evidence. In the last two decades mass spectrometry has revolutionized the analysis of proteins, allowing for thousands of peptides to be detected in a single analysis, including peptides containing single amino acid polymorphisms. Identification of these genetically variant peptides (GVP) allows for inference of the underlying non-synonymous SNP genotype. We have focused on hair proteins as a source of genetic information, with 240 genetically GVPs being discovered and validated. Using optimized processing a single hair shaft can obtain random match probabilities (RMPs) of up to 1 in 100 million. We show that GVP-inferred genotypes are not affected by the anatomical origin of the hair shaft or pigmentation. Harsh oxidation with peroxide does not affect RMPs. Importantly, GVP-inferred SNP genotypes are statistically compatible with STR-typing and *Alu* retroelements, with 90% of GVP-inferred SNPs being located greater than 10 million and 75 million bp from the nearest STR or *Alu* element respectively. We have shown separation of DNA and peptide workflows from the same samples. Recent work has shifted to the use of a targeted peptide assay. When data acquisition of GVPs was dynamically triggered by the appearance of a standard peptide this approach resulted in a 2.5 fold increase in sensitivity and increased confidence in peptide detection. Based on Monte Carlo modeling we predict this increase in sensitivity will result in RMPs in excess of 1 in 1 trillion from a single hair shaft. Proteomic genotyping can also be applied to any protein matrix, including fingermarks and bone. Proteomic genotyping therefore has potential to complement and enhance partial DNA typing and provide other options for investigators.