THE POTENTIAL AND CHALLENGE OF FORENSIC PROTEOMICS: WHAT IS NEEDED TO MEET THE DAUBERT STANDARD

Zach Goecker, Michelle Salemi, Brett Phinney, Glendon Parker, University of California, Davis

Forensic proteomics is a growing field with many potential applications. The last two decades have seen a revolution in the ability to detect and analyze protein populations. Proteomic mass spectrometry now results in highly complex datasets, comprised of peptide spectra, which often number in the tens of thousands. This information consists of peptide masses and the masses of matching peptide fragments. Because these spectra are specific and result from the order and composition of amino acids, detection can be used to infer the presence of a given protein and an originating gene. Proteomics can therefore provide significant insight into many scientific contexts including forensics. The identification of body fluids or tissues, or an originating species can be particularly relevant to a forensic context. Protein can also be a source of genetic information. Identification of peptides containing single amino acid polymorphisms can be used to infer a profile of non-synonymous SNPs in an individual. This information can be used to identify individuals, such as a calculated power of discrimination, or for forensic intelligence, such as calculating an ancestral likelihood.

Before proteomic mass spectrometry data can be used in a legal setting, however, the link between a specific spectrum and the originating amino acid sequence must be unambiguous and certain. Proteomics generally addresses this issue by not depending on any one spectrum. Typically two peptides are required to claim that a protein is in a sample. This is not an option for genetically variant peptides, where one spectrum must be sufficient to accurately infer a non-synonymous SNP. The standard proteomic quality measure, the false discovery rate, is inappropriate for a legal setting because it relies on decoy databases and quality scores of a whole peptide population; any one peptide may be an exception. However, genetically variant peptides have an additional metric; the genetic inferences can be specifically tested using standard DNA methods. Greater certainty can be obtained by the use of exogenous stable isotope peptides that have all of the metrics of the target peptide except for mass. This approach is often used in toxicology. The presence of an external standard allows us to characterize and compare the spectrum with that of endogenous peptides with high precision. The combination of direct DNA validation and external standards allow for unambiguous interpretation of mass spectra, confident construction of inferred SNP profiles, and would meet legal standards for evidence.