Individual Abstract Info

Session: Bioinformatics **Code:** ThP28 **Time Slot/Poster Number:** 442

Mass Spectral Disease Profiling: Better Biomarkers or Bust?

Scott A Kuzdzal[1]; Alvydas Mikulskis[1]; Mary Lopez[1]; Eva Golenko[1]; Joseph DiCesare[1]; Wayne Patton[1]; Lisa Sapp[1]; Guy della Cioppa[2]; Gershon Wolfe[2]; David Bennett[3]; Simon Melov[4];

[1]PerkinElmer Life & Analytical Sciences, Shelton, CT; [2]Predictive Diagnostics, Vacaville, CA; [3]Rush Alzheimer's Institute, Chicago , IL; [4]Buck Institute for Aging, Novato, CA;

Introduction:

Many proteomics researchers are abandoning the 'single marker' strategy and are developing integrated suites of algorithms to perform proteomics profiling directly from mass spectra. This approach represents a major paradigm shift in proteomics; the entire mass spectral profile contains important diagnostic information (rather than isolated, identified markers). The advantages are clear: the mass spectrometer can accurately measure proteins and peptides without the need for antibodies, so the assay development time is drastically reduced. This approach, however, requires a combination of effective, reproducible sample fractionation/enrichment strategies, sensitive, reproducible analytical detection systems and powerful bioinformatics algorithms. This presentation will compare Alzheimer's disease (AD) biomarker results obtained using both mass spectral profiling and traditional Peptide Mass Fingerprinting (PMF) techniques.

Methods:

Alzheimer's human brain (cortex) tissue, controls and 350 'blinded' sera were obtained from the Religious Order Study. Samples were fractionated using microscale fractionation protocols and differentially expressed protein spots were identified by differential gel electrophoresis. PMF identifications and mass spectral profiling experiments were performed on a MALDI Orthogonal-TOF mass spectrometer. A comprehensive suite of in silico machine learning technologies and advanced informatics tools was used to perform quality control steps, generate and score potential biomarkers, build an optimal biomarker model, and classify the disease state according to an optimized computational model.

Abstract:

Over 100 statistically significant, differentially expressed protein spots were identified using PMF methods and MALDI mass spectral profiling resulted in an Alzheimer's disease fingerprint that successfully classified AD samples from controls with high sensitivity (94%) and specificity (89%). These two approaches are complementary; the rapid profiling capabilities of spectral profiling enable more efficient sample fractionation/enrichment optimization and prime predictor selection for traditional methods (which, in turn, offer identification abilities).

---

close window