[S06.003] Identification of Novel Protein Biomarkers that Predict Amyotrophic Lateral Sclerosis Clinical Progression

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OBJECTIVE: These studies were designed to test the feasibility of using high-throughput protein fingerprint expression analysis for the identification of novel protein biomarkers that may be used as indexes of the initiation and/or progression of motor neuron degeneration inamyotrophic latereral sclerosis (ALS). **BACKGROUND:** Despite a long history of clinical and pathological studies, little is known about the molecular mechanisms underlying the pathologic features of ALS. Furthermore, the causes of ALS appear likely to be multi-factorial, and have been demonstrated to involve both genetic and environmental factors. The availability of specific biological indexes of clinical ALS would promote understanding of the pathogenetic mechanisms underlying ALS. **DESIGN/METHODS:** We used Ciphergene surface-enhanced laser desorption ionization mass spectrometry (SELDI-MS) technology to generate protein expression fingerprints from pre-banked cerebrospinal spinal fluid (CSF) samples of definitive ALS cases identified based on the El Escorial criteria. We then used Pearson correlation analysis to explore the predicative role of individual CSF protein species in ALS clinical progression based on ALS functional rating scale (ALSFRS). **RESULTS:** We found a series of novel potential protein biomarkers whose content in CSF significantly correlates with the rate of ALS clinical progression. In particular, we found that the CSF content of a novel 4.8-kDa protein species negatively charged at pH 8.0, among three biomarkers currently under characterization in our lab, increased as a function of the ALS clinical progression assessed by ALSFRS. Interestingly, we also found that two of our potential novel indexes of ALS clinical progression, including the 4.8-kDa protein species, were also detectable in serum. We are presently sequence identifying and generating quantitative ELISA assays for the currently identified biomarkers and exploring the consistency and reproducibility of our SELDI-MS fingerprinting analysis in predicting ALS-FRS rate of decline. **CONCLUSIONS:** Our studies strongly support the utility of using the high-throughput protein profiling for the identification of novel protein biomarkers (serum and CSF) that may be used as indexes of the initiation and/or progression of motor neuron degeneration in ALS.

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