Title: Using human cerebrospinal fluid samples collected in DATATOP study for biomarker discovery and validation in patients with Parkinson’s disease

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Abstract: An accurate diagnosis of Parkinson’s disease (PD) is difficult sometimes even in the best hands and the natural course of PD varies substantially. We have hypothesized that there are unique protein markers for both PD diagnosis and PD progression in human cerebrospinal fluid (CSF) (an ideal source for discovering biomarkers owing to its direct contact with the central nervous system). Indeed, we have quantitatively compared the CSF proteome of patients with PD, Alzheimer’s disease (AD), dementia with Lewy bodies (DLB) and age-matched controls. The CSF from AD and DLB were obtained at the Oregon Health Science University (OHSU) by one of our collaborators, Dr. Joseph Quinn. The clinical stages of AD and DLB were mild to moderately advanced at the time of the CSF was obtained, and only cases with final pathological confirmation were used. CSF of PD cases were obtained by Drs. Joseph Jankovic and Christopher Kenney at Baylor College of Medicine, Drs. Kathy Chung and Jay Nutt at OHSU, and Drs. James Leverenz and Cyrus Zabetian at the University of Washington School of Medicine (UWSM); all patients met NINDS’ criteria of probable PD, with good response to dopamine therapies, and within five years of initial diagnosis, i.e. at a relatively early stage of PD. CSF of control subjects were obtained by Dr. Elaine Peskind at UWSM, who is in charge of one of the largest human CSF banks in the country. Characterization and quality control, particularly the extent of blood contamination of CSF, was performed, and quantitative proteomics in conjunction with iTRAQ experiments were performed by the standard protocol. The results indicated that there were 72 proteins unique to PD patients and a combination of two verified markers (by Western blotting analysis of individual samples) appeared to be able to segregate PD patients not only from controls but also from patients with AD and DLB. The Specific Aims of our ongoing projects are two: 1) to investigate whether the discovered putative markers can be validated in a different yet larger population of patients in terms of their sensitivity/specificity in differentiating PD from other diseases as well as predicting PD progression, and 2) using the same technique as mentioned above to further explore PD progression markers in a cross-sectional and/or a longitudinal study, where PD patients at various stages will be utilized. Both types of experiments will be performed using the CSF samples collected in the DATATOP cohort.