Abstract

Objectives: Increased Tau phosphorylation followed by the accumulation of Tau in extracellular fluid (ECF) correlates with neurodegenerative diseases, including Alzheimer’s disease (AD). However, collection of ECF is invasive and inconvenient for use in longitudinal studies. We have developed ultrasensitive assays for measuring total Tau (tTau) and phosphorylated Tau (pTau).

Methods: MSD’s ultrasensitive assay format, S-PLEX®, uses MSD’s MULTI-ARRAY® electrochemiluminescence technology and is based on the principle that an increase in electrochemical current (ECL) is inversely proportional to analyte concentration. The ECL signal is generated by the oxidation of a label conjugated to the analyte. The signal is proportional to the amount of label that is oxidized, which is dependent on the amount of analyte present. The signal is measured using an array of electrodes, where each electrode is coated with a different antibody that specifically recognizes the analyte of interest. The signal from each electrode is measured and the concentration of the analyte is determined by comparing the signal to a standard curve.

Results: The new MSD® S-PLEX tTau and pTau(181) assays have a limit of detection (LOD) below 200 fg/mL and below 3000 fg/mL for pTau(231) based on full length Tau concentration. All assays have a dynamic range of at least 3 logs. The assays were developed as multi-format, with improved sensitivity over standard immunoassay formats. The assays’ improved sensitivity allows for quantitation of tTau and pTau in serum and plasma, and their utility has been demonstrated by measuring elevated levels in disease samples with Phospho-Tau Assay Specificity.

Conclusion: These assays allow quantitation of tTau and pTau181 in serum and plasma, providing a new tool for researching these important biomarkers of neurodegeneration.