Development and Analytical Validation of a Novel Assay for Measurement of Total Tau in Human CSF

Jill Dunty,1,2 Flora Berisha,1 Leonard Dzantiev,1 Adam Simon,1 Carol Gleeson,1 Olivia Wong,2 Mwamentu Mbwana,1 Sara Haiip,1 Gian Ning,1 Franklin Braffett,1 Sarah Robles,1 George Green,2 Robert Neely,2 Holly Soares,2 James Willbur,1 Pankaj Oberoi,1 David Stewart,1 Jacob N. Wohlstadter,1 and Paul Rhyme2

1 Meso Scale Discovery2 Bristol-Myers Squibb Company, Princeton, NJ; 2 Jacob N. Wohlstadter Enterprises, LLC, Yardley, PA

Abstract

Background: Measurement of total tau in CSF is critical for the diagnosis and monitoring of neurodegenerative diseases such as Alzheimer’s disease (AD). Current methods of measuring total tau in CSF have limitations, including lack of automation, sensitivity, and specificity.

Methods: A new assay was developed and analytically validated to measure total tau in human CSF. The assay was built using highly-evolved detection and capture antibodies and an automated platform. The assay was validated using well-curated CSF samples with a range of total tau concentrations. The assay was compared to an already validated assay using a different method to determine its performance characteristics.

Results: The new assay exhibited excellent sensitivity, specificity, and precision. The %CV of the calculated concentration was less than 20% and the percent recovery of the standard was within 80–120%. The assay was able to detect total tau in CSF levels down to 5 pg/mL with a %CV of less than 20%.

Conclusions: The new assay provides a reliable, sensitive, and specific method for measuring total tau in human CSF, which can be used for the early detection and monitoring of neurodegenerative diseases.

Keywords: total tau, CSF, assay validation, Alzheimer’s disease