

Description

Tau is a microtubule-stabilizing protein primarily localized in central nervous system neurons, but also expressed at low levels in astrocytes and oligodendrocytes. Tau consists of six isoforms in the human brain, with molecular weights of 48,000 to 67,000 daltons depending on isoform. Tau elevation is observed in the cerebrospinal fluid (CSF) of patients with neurodegenerative disease and head injuries, suggesting its extracellular release during neuronal damage and a role as a biomarker with specificity for brain injury. Potential movement of elevated CSF tau across the blood-brain barrier presents a possibility that measurements of tau in blood could provide a convenient peripheral window into brain/CSF status. Studies of tau in serum and plasma have been hampered by its low abundance (typically low pg/mL), and there are relatively few reports characterizing the appearance of tau in blood or evaluating the usefulness of this biomarker for brain injury assessment. Recent reports using digital immunoassay technology have shown elevation in peripheral tau associated with hypoxic brain injury, concussed hockey players, and repetitive minimal head injury in Olympic boxing. The Simoa™ Human Total Tau assay uses a combination of monoclonal antibodies that react with both normal and phosphorylated tau. With an epitope in the midregion of the molecule, the assay recognizes all tau isoforms.

Calibration Curve: Calibrator concentrations and Lower Limit of Quantification depicted.

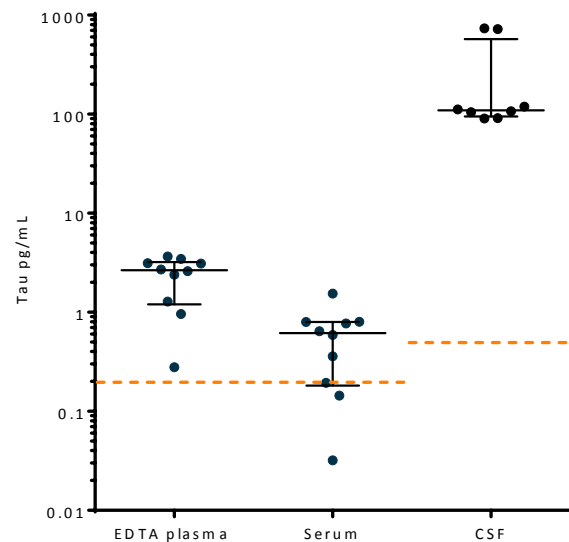
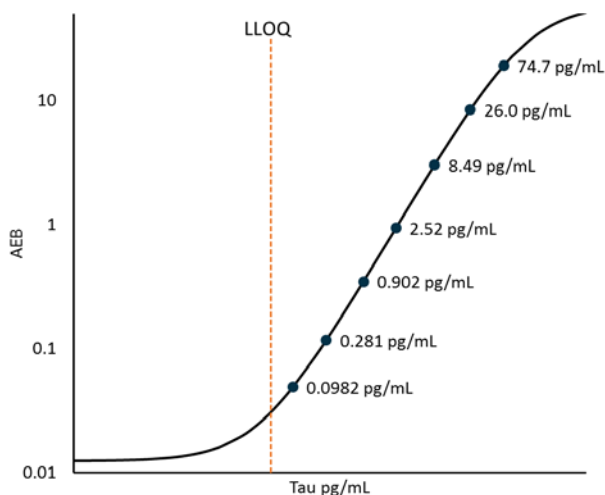
Lower Limit of Quantification (LLOQ): Triplicate measurements of serially diluted calibrator were read back on the calibration curve over 6 runs each for 1 reagent lot across 2 instruments (6 runs total).

Limit of Detection (LOD): Calculated as 2.5 standard deviations from the mean of background signal read back on each calibration curve over 6 runs each for 1 reagent lot across 2 instruments (6 runs total).

LLOQ	0.0491 pg/mL pooled CV 9% mean recovery 95%
LOD	0.0146 pg/mL range 0.0061-0.0278 pg/mL
Dynamic range (serum and plasma)	0- ~400 pg/mL
Dynamic range (CSF)	0- ~1000 pg/mL
Diluted Sample volume*	152 µL per measurement
Tests per kit	96

*Serum and Plasma diluted 1:4 and CSF diluted 1:10. See Kit Instruction for details

Endogenous Sample Reading: Healthy donor matched EDTA plasma (n=10), and serum (n=10), and unmatched CSF samples (n=10) were measured. Bars depict median with interquartile range. Orange lines represent functional LLOQ.



Sample Type	Mean Tau pg/mL	Median Tau pg/mL	% Above LOD
Serum	0.785*	0.648	70%
Plasma	2.36	2.65	100%
CSF	260	109	100%

*Values below LLOQ are not included in the mean

The Simoa Tau assay kit is formulated for use on either the SR-X or HD-1 platform. Minor differences in performance claims between the HD-1 and SR-X may be observed when comparing datasheets for the two different platforms, due to experiments run at different time-points with different reagent lots and different samples. Data in this document was obtained from runs on the SR-X platform unless otherwise noted.

Precision: Measurements of 3 serum-based panels and 2 calibrator based controls. Triplicate measurements were made for 6 runs each for 1 reagent lot across 2 instruments (6 runs total, 18 measurements).

Sample	Mean (pg/mL)	Within run CV	Between run CV	Between inst CV
Control 1	1.15	8.4%	13.3%	17.2%
Control 2	59.2	11.5%	7.8%	2.6%
Panel 1	1.10	5.9%	10.5%	10.5%
Panel 2	1.40	10.2%	8.3%	4.3%
Panel 3	60.9	9.0%	10.5%	1.9%

Note: Data in the following sections were obtained using the HD-1 Analyzer.

Spike and Recovery: 4 serum samples were spiked at high and low concentrations within the range of the assay and analyzed on HD-1.

Dilution Linearity: 1 endogenous EDTA plasma sample was diluted 2X serially to 32x with Sample Diluent. 1 endogenous CSF sample was diluted 2X serially to 64x with Sample Diluent.

Spike and Recovery (Serum/Plasma)	Mean = 85% Range: 40–121%
Spike and Recovery (CSF)	Mean = 102% Range: 102–103%
Serum Dilution Linearity (32x)	Mean = 113% Range: 110–125%
CSF Dilution Linearity (64x)	Mean = 93% Range: 82–107%