Overview

Useful For
Quantitative measurement of total Tau in human cerebrospinal fluid

Method Name
Chemiluminescent Immunoassay

NY State Available
Yes

Reporting Name
Total Tau, CSF

Aliases
Total-Tau
tTau

Specimen

Specimen Type
CSF

Specimen Required
Container/Tube: Sarstedt Aliquot Tube, 5 mL 62.504.040
Specimen Volume: 1 mL
Collection Instructions:
1. Perform lumbar puncture and discard the first 1 to 2 mL of cerebrospinal fluid (CSF).
2. Collect CSF directly into one of the listed collection tubes
Note: Polypropylene collection tubes must be used. Polystyrene collection tubes are not acceptable.
3. Inspect specimen for visible blood contamination:
a. If bloody, centrifuge specimen and transfer supernatant to a new one of the listed collection tubes prior freezing and sending to laboratory. The supernatant, not the cellular material, is used for analysis.
b. If specimen is clear, centrifugation is not necessary.
4. Freeze sample upright prior to placing in transport container.

Specimen Minimum Volume
0.5 mL

Reject Due To

Gross hemolysis	Reject
Thawing	Cold OK; Warm reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen	90 days	

Clinical & Interpretive

Clinical Information
Two neuropathologic features observed in the brain of patients with Alzheimer disease (AD) dementia are the presence of plaques composed of beta-amyloid (Abeta) peptides and intracellular neurofibrillary tangles containing hyperphosphorylated Tau (tubulin-associated unit) proteins. These 2 groups of molecules are the most established biomarkers of the disease used in clinical and research practice.
Measuring of total Tau (t-Tau) proteins in cerebrospinal fluid (CSF) may be used to assess the presence of amyloid pathology. However, t-Tau is not a specific biomarker of AD, and it mostly represents the amount of neuronal and axonal damage making it a biomarker of neurodegeneration.
The t-Tau assay used here has been reported to have an area under the receiver operating characteristic curve of 0.80 (95%CI 0.70–0.89) for detection for an abnormal amyloid-positron emission tomography as assessed by visual read.(1)
High CSF t-Tau protein concentrations are also found in other neurodegenerative diseases such as prion disease or Creutzfeldt-Jakob disease (CJD). In this situation, an elevated t-Tau concentration with an increased t-Tau to phosphorylated Tau ratio have a very high specificity for the differential diagnosis of CJD.

Reference Values
< or =456 pg/mL

Interpretation
A cutoff of 456 pg/mL has an 75% positive percent agreement, 83% negative percent agreement, and 78% overall percent agreement with amyloid-positron emission tomography (PET).(1)
A total Tau concentration less than or equal to 456 pg/mL will be most consistent with a negative amyloid-PET. A total Tau concentration greater than 456 pg/mL will be most consistent with a positive amyloid-PET.

Cautions
Total-Tau (t-Tau) results must be interpreted in conjunction with other diagnostic tools, such as neurological examination, neurobehavioral tests, imaging, and routine laboratory tests.
In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.
Results obtained with different assay methods or kits may be different and cannot be used interchangeably.

Clinical Reference
1. Alcolea D, Pegueroles J, Munoz L, et al. Agreement of amyloid PET and CSF biomarkers for Alzheimer's disease on Lumipulse. Ann Clin Transl Neurol. 2019;6(9):1815-1824
2. Leitao MJ, Silva-Spinola A, Santana I, et al. Clinical validation of the Lumipulse G cerebrospinal fluid assays for routine diagnosis of Alzheimer's disease. Alzheimers Res Ther. 2019;11(1):91. Published 2019 Nov 23. doi:10.1186/s13195-019-0550-8
3. Gobom J, Parnetti L, Rosa-Neto P, et al. Validation of the LUMIPULSE automated immunoassay for the measurement of core AD biomarkers in cerebrospinal fluid. Clin Chem Lab Med. 2021;60(2):207-219. Published 2021 Nov 15. doi:10.1515/cclm-2021-0651
4. Campbell MR, Ashrafzadeh-Kian S, Petersen RC, et al. P-tau/Abeta42 and Abeta42/40 ratios in CSF are equally predictive of amyloid PET status. Alzheimer's Dement. 2021;13:e12190
5. Chang BK, Day GS, Graff-Radford J, et al. Alzheimer's disease cerebrospinal fluid biomarkers differentiate patients with Creutzfeldt-Jakob disease and autoimmune encephalitis. Eur J Neurol. 2022;29(10):2905-2912
6. Shir D, Lazar EB, Graff-Radford J, et al. Analysis of clinical features, diagnostic tests, and biomarkers in patients with suspected Creutzfeldt-Jakob Disease, 2014-2021. JAMA Netw Open. 2022;5(8):e2225098

7. Skillback T, Rosen C, Asztely F, Mattsson N, Blennow K, Zetterberg H. Diagnostic performance of cerebrospinal fluid total tau and phosphorylated tau in Creutzfeldt-Jakob disease: results from the Swedish Mortality Registry. JAMA Neurol. 2014;71(4):476-83

Performance

Method Description
The Lumipulse G Total Tau is an assay system for the quantitative measurement of total Tau in cerebrospinal fluid (CSF) specimens based on chemiluminescent immunoassay technology by a specific two-step sandwich immunoassay method on the Lumipulse G System. The specimen and biotinylated antibody solution are both added to the antibody coated particle solution. The total Tau in the specimen specifically binds to anti-total Tau monoclonal mouse antibody on the particles and biotinylated mouse antibody. Biotinylated antibody-antigen immunocomplexes are formed. The particles are washed and rinsed to remove unbound materials. Alkaline phosphatase labeled streptavidin specifically binds to biotinylated immuno-complexes on the particles. The particles are washed and rinsed to remove unbound materials. Substrate solution is added and mixed with the particles. 3-(2'-Spiroadamantyl)-4-methoxy-4-(3-phosphoryloxy)-phenyl-1,2-dioxetane (AMPPD) contained in the substrate solution is dephosphorylated by the catalysis of alkaline phosphatase indirectly conjugated to particles. Luminescence (at a maximum wavelength of 477 nm) is generated by the cleavage reaction of dephosphorylated AMPPD. The luminescent signal reflects the amount of total Tau present in the sample (Package insert: Lumipulse G Total Tau. Fujirebio Inc; 01/2023).

Day(s) Performed
Tuesday. Testing may be performed on additional days per client request.

Report Available
1 to 7 days

Specimen Retention Time
90 days

Performing Laboratory Location
Rochester

CLIA Laboratory Number
24D1040592

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.