Plasma p-tau181

- Diagnostic dynamic contrast-enhanced magnetic resonance imaging blood-brain barrier assessment combined with plasma biomarkers for mild cognitive impairment
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Plasma p-tau181 is a biomarker used to measure the level of a specific type of tau protein in the blood. Tau protein is found in the brain and helps to stabilize the structure of neurons. However, in conditions like Alzheimer's disease, tau protein can become abnormal and form tangles within the brain, which can lead to the death of neurons and cognitive decline.

Recent research has shown that levels of p-tau181 in the blood can reflect the presence of tau tangles in the brain, making it a potential biomarker for Alzheimer's disease. Studies have suggested that plasma p-tau181 levels may be able to distinguish between Alzheimer's disease and other forms of dementia and may be useful in tracking disease progression over time.

However, more research is needed to validate the use of plasma p-tau181 as a diagnostic tool for Alzheimer's disease and to determine the best way to interpret and use this biomarker in clinical practice.

Therriault et al. assessed the diagnostic performance of p-tau181, p-tau217, and p-tau231 in plasma and CSF in 174 individuals evaluated by dementia specialists and assessed with amyloid-PET and tau-PET. Receiver operating characteristic (ROC) analyses assessed the performance of plasma and CSF biomarkers to identify amyloid-PET and tau-PET positivity.

Plasma p-tau biomarkers had lower dynamic ranges and effect sizes compared to CSF p-tau. Plasma p-tau181 (AUC = 76%) and p-tau231 (AUC = 82%) assessments performed inferior to CSF p-tau181 (AUC = 87%) and p-tau231 (AUC = 95%) for amyloid-PET positivity. However, plasma p-tau217 (AUC = 91%) had diagnostic performance indistinguishable from CSF (AUC = 94%) for amyloid-PET positivity.

Discussion: Plasma and CSF p-tau217 had an equivalent diagnostic performance for biomarker-

defined AD. Our results suggest that plasma p-tau217 may help reduce the need for invasive lumbar punctures without compromising accuracy in the identification of AD.

Highlights: p-tau217 in plasma performed equivalent to p-tau217 in CSF for the diagnosis of AD, suggesting the increased accessibility of plasma p-tau217 is not offset by lower accuracy. p-tau biomarkers in plasma had lower mean fold-changes between amyloid-PET negative and positive groups than p-tau biomarkers in CSF. CSF p-tau biomarkers had greater effect sizes than plasma p-tau biomarkers when differentiating between amyloid-PET positive and negative groups. Plasma p-tau181 and plasma p-tau231 performed worse than p-tau181 and p-tau231 in CSF for AD diagnosis [1)]

Frank et al. from the Boston University School of Medicine examined the ability of plasma hyperphosphorylated tau (p-tau)181 to detect cognitive impairment due to Alzheimer's disease (AD) independently and in combination with plasma total tau (t-tau) and neurofilament light (NfL).

Plasma samples were analyzed using the Simoa platform for 235 participants with normal cognition (NC), 181 with mild cognitive impairment due to AD (MCI), and 153 with AD dementia. Statistical approaches included multinomial regression and Gaussian graphical models (GGMs) to assess a network of plasma biomarkers, neuropsychological tests, and demographic variables.

Plasma p-tau181 discriminated AD dementia from NC, but not MCI, and correlated with dementia severity and worse neuropsychological test performance. Plasma NfL similarly discriminated diagnostic groups. Unlike plasma NfL or t-tau, p-tau181 had a direct association with cognitive diagnosis in a bootstrapped GGM.

These results support plasma p-tau181 for the detection of Alzheimer's disease dementia and the use of blood-based biomarkers for optimal disease detection [2)].

Results suggest that in elderly individuals without dementia at baseline, plasma p-tau181 biomarkers were associated with greater memory decline and rates of clinical progression to dementia. Plasma p-tau181 improved prediction of memory decline above a model with currently available clinical and genetic data. While the clinical importance of this improvement in the prediction of memory decline is unknown, these results highlight the potential of plasma p-tau181 as a cost-effective and scalable Alzheimer's disease biomarker [3)]

Plasma p-tau231 is a promising novel biomarker of emerging AD pathology with the potential to facilitate clinical trials to identify vulnerable populations below the PET threshold of amyloid-β positivity or apparent entorhinal tau deposition. [4)].

The study of Karikari et al. adds significant weight to the growing body of evidence in the use of plasma p-tau181 as a non-invasive diagnostic and prognostic tool for AD, regardless of clinical stage, which would be of great benefit in clinical practice and a large cost-saving in clinical trial recruitment. [5)]

O'Connor et al. investigated the timing of p-tau181 changes using 153 blood samples from 70 individuals in a longitudinal study of familial AD (FAD). Plasma p-tau181 was measured, using an in-house single-molecule array assay. We compared p-tau181 between symptomatic carriers, presymptomatic carriers, and non-carriers, adjusting for age and sex. We examined the relationship between p-tau181 and neurofilament light and estimated years to/from symptom onset (EYO), as well as years to/from the actual onset in asymptomatic subgroup. In addition, we studied associations between p-tau181 and clinical severity, as well as testing for differences between genetic subgroups. Twenty-four were presymptomatic carriers (mean baseline EYO -9.6 years) while 27 were non-carriers. Compared with non-carriers, plasma p-tau181 concentration was higher in both symptomatic ($p < 0.001$) and presymptomatic mutation carriers ($p < 0.001$). Plasma p-tau181 showed considerable intra-individual variability but individual values discriminated symptomatic (AUC 0.93 [95% CI 0.85-0.98]) and presymptomatic (EYO ≥ -7 years) (AUC 0.86 [95% CI 0.72-0.94]) carriers from non-carriers of the same age and sex. From a fitted model, there was evidence ($p = 0.050$) that p-tau181 concentrations were higher in mutation carriers than non-carriers from 16 years prior to estimated symptom onset. Our finding that plasma p-tau181 concentration is increased in symptomatic and presymptomatic FAD suggests potential utility as an easily accessible biomarker of AD pathology. [6].

1)

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2)

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3)

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4)

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5)

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6)

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