

**Tau** and **Amyloid beta** in CSF represents the earliest and most intensively studied biomarkers.

**CSF** is probably the most informative fluid in **biomarkers** discovery for neurodegenerative disease prognosis. CSF has more physical contact with brain than any other fluids, as it is not separated from the brain by tightly regulated blood brain barrier (BBB). As a result, proteins or peptides that may be directly reflective of brain specific activities as well as disease pathology would most likely diffuse into CSF than into any other bodily fluid. These proteins and metabolites can serve as excellent biomarkers of AD as well as other neurodegenerative diseases. In early course of AD, for an example of MCI, when the correct diagnosis is most difficult, CSF biomarkers would be valuable in particular <sup>1)</sup>.

Besides tau and A $\beta$ , neuronal and synaptic proteins could also be used as CSF biomarkers in AD. For example, Visinin-like protein 1 (VLP-1), a calcium sensor protein was shown to be significantly increased in the CSF of AD subjects compared to controls. It is believed to seep out from dented neurons <sup>2)</sup>.

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Longitudinal **CSF biomarker** patterns consistent with Alzheimer Disease (AD) are first detectable during early middle age and are associated with later **amyloid** positivity and **cognitive decline**. Such measures may be useful for targeting middle-aged, asymptomatic individuals for therapeutic trials designed to prevent cognitive decline <sup>3)</sup>.

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**SP-G** is a potential new **cerebrospinal fluid biomarker**, possibly not only reflecting aspects of CNS innate immune responses, but also rheo-dynamically relevant changes of CSF composition, associated with CSF malabsorption. However, further studies are warranted to validate this findings and increase insight into the physiological importance of SP-G in the CNS <sup>4)</sup>.

## Cerebrospinal fluid biomarker for dementia

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<sup>1)</sup>

Blennow K, Hampel H, Weiner M, Zetterberg H. Cerebrospinal fluid and plasma biomarkers in Alzheimer disease. *Nature Reviews Neurology*. 2010;6(3):131–144.

<sup>2)</sup>

Lee J-M, Blennow K, Andreasen N, et al. The brain injury biomarker VLP-1 is increased in the cerebrospinal fluid of Alzheimer disease patients. *Clinical Chemistry*. 2008;54(10):1617–1623.

<sup>3)</sup>

Sutphen CL, Jasielec MS, Shah AR, Macy EM, Xiong C, Vlassenko AG, Benzinger TL, Stoops EE, Vanderstichele HM, Brix B, Darby HD, Vandijck ML, Ladenson JH, Morris JC, Holtzman DM, Fagan AM. Longitudinal Cerebrospinal Fluid Biomarker Changes in Preclinical Alzheimer Disease During Middle Age. *JAMA Neurol*. 2015 Sep;72(9):1029-42. doi: 10.1001/jamaneurol.2015.1285. PubMed PMID: 26147946; PubMed Central PMCID: PMC4570860.

<sup>4)</sup>

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