Blood biomarkers for Alzheimer's disease

- A secondary analysis of cortical atrophy and plasma amyloid β patterns in older patients with cognitive frailty undergoing elective surgery
- Sarcopenia index is associated with Alzheimer's disease, mild cognitive impairment and their mortality in Chinese adults aged 65 and older
- Accuracy of blood-based neurofilament light to different genetic frontotemporal dementia from primary psychiatric disorders
- Integrative analysis of T cell-associated markers in Ewing sarcoma reveals prognostic signatures and immune dynamics
- The aggregation propensity of Tau and amyloid-beta in Alzheimer's disease
- Tau protein aggregation: A therapeutic target for neurodegenerative diseases
- Enrichment of extracellular vesicles using Mag-Net for the analysis of the plasma proteome
- Proteomic analysis of Down syndrome cerebrospinal fluid compared to late-onset and autosomal dominant Alzheimers disease

see also Cerebrospinal fluid biomarkers for Alzheimer's disease.

Blood biomarkers have emerged as accessible, cost-effective, and highly promising tools for advancing Alzheimer's disease diagnosis. However, transitioning from cerebrospinal fluid biomarkers to blood biomarkers-eg, to verify amyloid beta pathology-requires careful consideration.

Blood biomarkers for Alzheimer's disease (AD) are an area of active research aimed at improving early diagnosis and monitoring of the disease. Here are some of the key blood biomarkers currently being investigated:

Amyloid-beta (Aβ): Studies have shown that specific forms of amyloid-beta (such as Aβ42 and Aβ40) can be measured in blood plasma. Lower levels of Aβ42 relative to Aβ40 may indicate the presence of amyloid plaques in the brain, a hallmark of AD.

Tau Protein: Hyperphosphorylated tau protein (p-tau) in the blood is another promising biomarker. Elevated levels of p-tau have been associated with AD and may indicate neurodegeneration.

Neurofilament Light Chain (NfL): This biomarker reflects neuronal injury and has been shown to be elevated in various neurodegenerative diseases, including AD. High levels of NfL in the blood correlate with cognitive decline.

Inflammatory Markers: Various inflammatory cytokines and proteins, such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), are being studied as potential biomarkers due to their roles in neuroinflammation associated with AD.

Lipid Profiles: Changes in lipid metabolism, including alterations in certain fatty acids and lipoproteins, have been linked to AD. Research is ongoing to understand these associations better.

Metabolomics: Profiling metabolites in the blood has shown promise for identifying metabolic changes

associated with AD. Some studies have suggested that specific metabolites may serve as biomarkers for early detection.

Other Proteins: Other candidate proteins, such as clusterin and apolipoprotein E (ApoE), are being investigated for their roles in AD pathology and potential as blood biomarkers.

Current Limitations and Future Directions

While these biomarkers show promise, their clinical utility is still under investigation. Challenges include variability in biomarker levels due to factors like age, sex, and comorbidities. Future research is focusing on validating these biomarkers in larger, diverse populations and establishing standardized testing methods to ensure reliable and reproducible results.

The ultimate goal is to develop a blood test that can assist in the early diagnosis of Alzheimer's disease, enabling timely intervention and management strategies.

Schöll et al. highlights the main challenges in the implementation of blood biomarkers for Alzheimer's disease in different possible contexts of use. Despite the robustness of measuring blood biomarker concentrations, the widespread adoption of blood biomarkers requires rigorous standardization efforts to address inherent challenges in diverse contexts of use. The challenges include understanding the effect of pre-analytical and analytical conditions, potential confounding factors, and comorbidities that could influence outcomes of blood biomarkers and their use in diverse populations. Additionally, distinct scenarios present their own specific challenges. In memory clinics, the successful integration of blood biomarkers in diagnostic tests will require well-established diagnostic accuracy and comprehensive assessments of the effect of blood biomarkers on the diagnostic confidence and patient management of clinicians. In primary care settings, and even more when implemented in population-based screening programmes for which no experience with any biomarkers for Alzheimer's disease currently exists, the implementation of blood biomarkers will be challenged by the need for education of primary care clinical staff and clear guidelines. However, despite the challenges, blood biomarkers hold great promise for substantially enhancing the diagnostic accuracy and effectively streamlining referral processes, leading to earlier diagnosis and access to treatments. The ongoing efforts that are shaping the integration of blood biomarkers across diverse clinical settings pave the way towards precision medicine in Alzheimer's disease [1)].

1)

Schöll M, Verberk IMW, Del Campo M, Delaby C, Therriault J, Chong JR, Palmqvist S, Alcolea D. Challenges in the practical implementation of blood biomarkers for Alzheimer's disease. Lancet Healthy Longev. 2024 Sep 26:100630. doi: 10.1016/j.lanhl.2024.07.013. Epub ahead of print. PMID: 39369727.