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Analyzing a multifunctional protein clustering for high-performance Alzheimer diagnosis

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Alzheimer's disease (AD) is a neurodegenerative progressive disorder and is the most common cause of dementia. AD affects the parts of the brain that control memory, thought, and language. The disturbances of cognitive abilities and memory loss are serious enough to disrupt everyday life. Currently, there is no approved medication that can treat and cure AD. Early detection of AD is becoming a major issue and is gaining worldwide attention. Since AD is progressive, a convenient, low-cost, and accurate detection system helps to identify the early stages of AD and provides better treatment options to improve patients' lives. Current diagnostic methods, such as cerebrospinal fluid (CSF) tests and neuroimaging techniques, are costly and difficult for most people to access. Research is ongoing to develop a highly sensitive AD biosensor with suitable biomarkers.

Various new biomarkers have been identified by researchers for diagnosing and therapeutic purposes for AD. Amyloid beta (Aβ) misfolding and aggregation is one possible process in the brains of AD patients. Aβ monomers (AβO) are converted into Aβ oligomers and fibrils (Sun et al., 2018). There is a significant association between the neurotoxic effects of AβO and the severity of AD. Studies further confirmed that patients have higher levels of AβO than normal individuals. Furthermore, the level of AβO in CSF can identify disease progression at earlier stages and is considered one of the well-known biomarkers for AD (Fig. 1). In addition to Aβ, AD is strongly linked with the accumulation of clumps in specific brain regions caused by the protein tau (Ng et al., 2019). In neurons, alpha-synuclein is abundant at presynaptic terminals, and tau is a microtubule-associated protein found in axons. They have a propensity to create pathogenic aggregates, which are believed to be the main factor causing AD. Since tau in CSF is a marker of neuronal death, it can be elevated in both atypical and non-AD dementia phenotypes; an increase in pTau is more specific to AD pathology in both atypical and typical presentations. Additionally, the dopaminergic system is frequently linked to the progressive form of AD and may play a role in the causes of cognitive decline (Pan et al., 2019). Furthermore, neurofilament light chain (NfL), a neuronal cytoplasmic protein that is strongly expressed in myelinated axons, is a marker of neurological disorders and can be used to distinguish between AD-related cognitive loss and other illnesses. An increase in NfL in CSF and plasma is also indicative of neurological disorders. Other biomarkers, such as chitinase 3-like 1, neurogranin, and glial fibrillary acidic protein, are under investigation.

Sensing the levels of these biomarkers in the CSF or plasma aids in the early identification of AD and in monitoring the condition during treatment. Various biosensors with different probes have been developed for quantifying AD biomarkers at lower levels. Researchers introduced dual probes with aptamers and antibodies to quantify Aβ levels in the CSF. Both the antibody and aptamer were immobilized on gold nanourchins and attached to a carbon nanohorn-modified interdigitated electrode sensor. These dual probes attracted Aβ from the CSF and identified levels as low as 10 fM (Qiu et al., 2021). Similarly, a highly sensitive ELISA assay was developed to identify Aβ in the CSF. Aptamer-immobilized gold nanoparticles were attached to a graphene-modified ELISA polystyrene plate through a chemical linker. An aptamer-antibody sandwich assay was then conducted, and this sensing system lowered the detection limit of Aβ to 20 pM (Zhao et al., 2021). Like Aβ, researchers have developed various biosensors for identifying the fibril formation of alpha-synuclein. Anti-alpha-synuclein was attached to the surface of gold nanoparticles and immobilized on a single-walled carbon nanotube-modified electrode. Voltammetry analysis identified fibril-formed alpha-synuclein on the antibody-modified surfaces at concentrations as low as 100 fM (Zhang et al., 2020). This lower level of α-synuclein identification helps to diagnose the disease progression of PD. In another research, the biomarker NfL was identified using an immunosensor on an interdigitated electrode. Anti-NfL was conjugated with gold nanourchins and attached to the electrode through amine modification, identifying the NfL antigen at levels as low as 1 pM. The gold nanourchins enhanced antibody immobilization on the sensing electrode and lowered the detection limit of NfL (Li et al., 2021). This nanomaterial-modified biosensor identifies the PD biomarker at its lower level and provides new data for understanding and diagnosing AD in clinical samples.

Declaration of competing interest

The authors declare that they have no known competing financial

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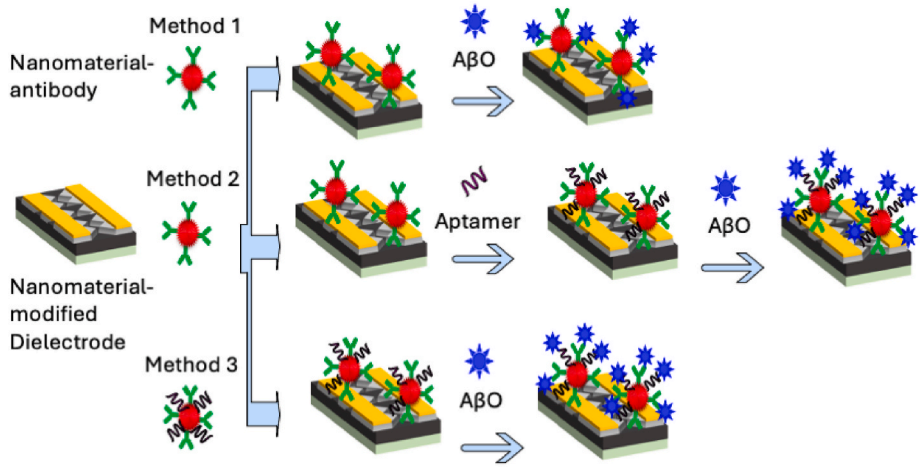

Fig. 1. Sensing strategies for Alzheimer detection. Methods involving antibody or aptamer and their combinations as dual detections are displayed. Presence of nanomaterials enhance the performance of detection.

interests or personal relationships that could have appeared to influence the work reported in this paper.

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