Progress on early detection of Alzheimer's disease

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Inside the body, some seemingly harmless proteins have sinister potential. In the case of Alzheimer's disease, the amyloid-beta (Aβ) protein, which is vital for brain growth, can become tainted and destroy

cells, which leads to forgetfulness and memory loss. Proteins are neat little things that can only perform their functions if folded properly. Thus, the misfolding and deposition of amyloid beta in the brain is the main hallmark of Alzheimer's disease.

"One of the drivers of Alzheimer's pathogenesis is the production of soluble oligomeric Aβ, which could potentially serve as a biomarker of Alzheimer's disease," said Tianfu Wu, University of Houston associate professor of biomedical engineering. Oligomeric proteins are comprised of several protein chains or subunits packed tightly together.

Since 1959, the fluorescent dye thioflavin-T (ThT) has been a widely used "gold standard" for selectively staining and identifying amyloid fibrils, which result from the self-assembly of proteins into those large groups. However, due to the charge and emission wavelength (less than 650 nm) of ThT, the in-vivo use is limited. In addition, ThT can detect only the fibrillar form of Aβ, but not the oligomeric forms.

That's why a new probe for in-vivo detection of the oligomeric form of Aβ is highly desirable for the early diagnosis of Alzheimer's disease, and that's what Wu and collaborators have been creating.

"We synthesized a near-infrared fluorescence-imaging probe to detect both soluble and insoluble Aβ. It not only binds oligomeric Aβ but also interposes self-assembly of Aβ," reports Wu in the journal *Alzheimer's and Dementia*. "This work holds great promise in the early diagnosis of Alzheimer's and may provide an alternative way to prevent and intervene in Alzheimer's disease and other amyloidosis."

That couldn't come a moment too soon. According to the Alzheimer's Association, more than 6 million Americans are living with Alzheimer's. By 2050, this number is projected to rise to nearly 13 million.

No real prevention and treatment of this chronic, degenerative brain disease exists; only five drugs are approved by the U.S. Food and Drug Administration to treat it, and they are all palliative. Unfortunately, these medications are not able to alleviate pathological changes or delay disease progression.

"It is notable that the lack of early and accurate diagnosis of Alzheimer's disease and disease surveillance further hinders the development of therapeutic drugs," said Wu. "Our hope is this new probe will help us detect the disease early and form targets for prevention and progression."

More information: Li Quan et al, A near-infrared probe for detecting and interposing amyloid beta oligomerization in early Alzheimer's disease, *Alzheimer's & Dementia* (2022). DOI: 10.1002/alz.12673

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