

# New smart technology can make diagnosis of AD more accessible

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A novel smartphone-enabled platform employing a fluorescence-responsive tiny molecule as a probe offers a simple, cost-effective, and accessible approach for the detection of the Alzheimer's disease (AD) biomarker amyloid- $\beta$  ( $A\beta$ ).

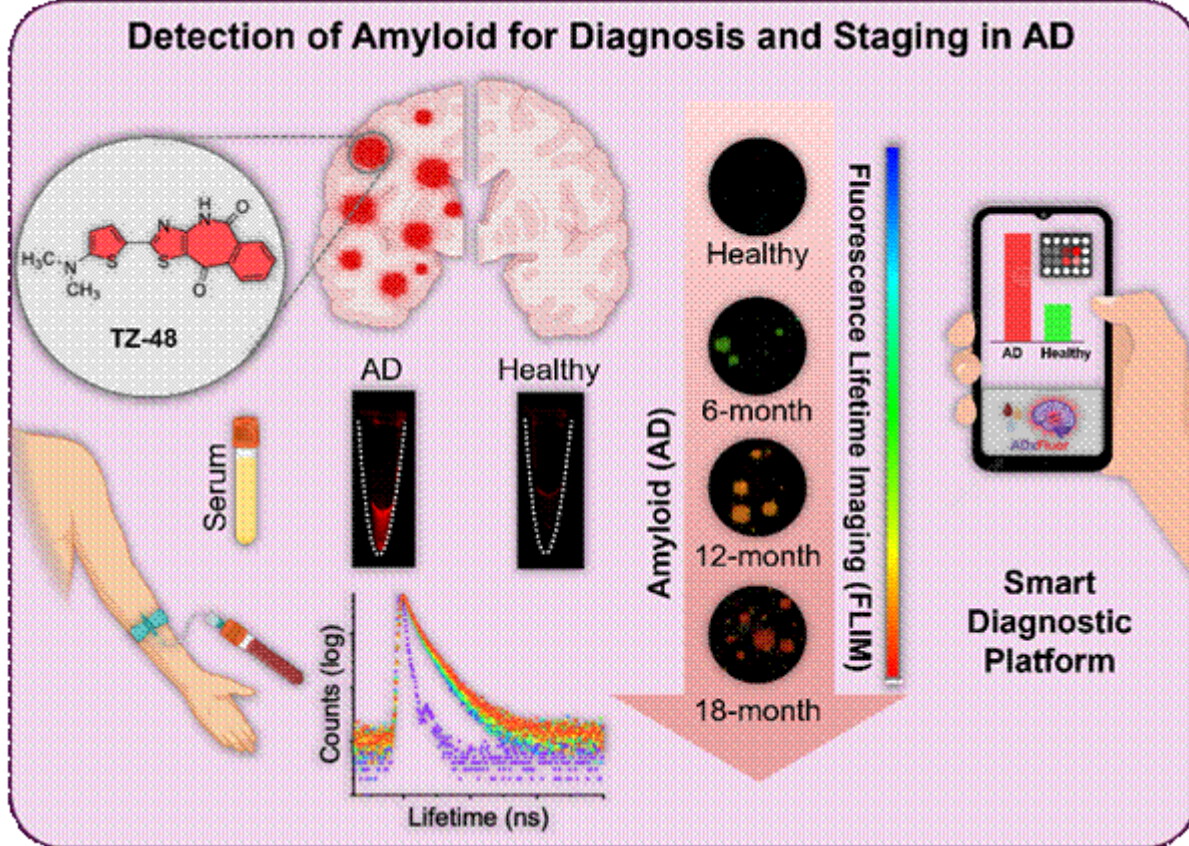
Upon interaction with  $A\beta$ , the tiny molecule called TZ-48 undergoes changes in fluorescence intensity, which are captured and quantified using a dedicated smartphone application. This enables rapid and user-friendly detection, with potential applications in the screening and staging of AD.

AD is a progressive neurodegenerative disorder characterized by memory loss, cognitive decline, and behavioural impairment. Central to its pathology is the misfolding and aggregation of amyloid- $\beta$  ( $A\beta$ ), which self-assembles into fibrils and deposits as extracellular plaques that trigger neurotoxic cascades leading to synaptic dysfunction and neurodegeneration.

The National Institute on Aging-Alzheimer's Association (NIA-AA) framework identifies  $A\beta$ , tau, and neurodegeneration as core biomarkers for definitive AD diagnosis across brain, cerebrospinal fluid (CSF), and blood. Importantly,  $A\beta$  pathology is an early and AD-specific biomarker, making  $A\beta$  a more reliable diagnostic indicator. Although positron emission tomography (PET) and magnetic resonance imaging (MRI) provide valuable diagnostic information, their high cost, need for specialized infrastructure, technical expertise, and limited accessibility restrict widespread use. Blood-based assays targeting  $A\beta$  and tau, have emerged as promising alternatives, but are expensive and complex. These limitations highlight the need for simple, sensitive, scalable diagnostic platforms capable of early and accurate detection of  $A\beta$  for AD diagnosis.

Fluorescence lifetime imaging microscopy (FLIM) has emerged as a powerful sensing modality because fluorescence lifetime is largely independent of probe concentration and photobleaching, enabling robust detection of biomarkers and enhancing diagnostic precision.

Scientists at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), an autonomous institute of the Department of Science and Technology, have developed a smart fluorescence lifetime-responsive probe that enables highly selective, sensitive, and differential detection of  $A\beta$  fibrils ( $A\beta_f$ ) through turn-on fluorescence and distinct lifetime signatures.



The probe called TZ-48 published in the journal ACS Chemical Neuroscience exhibits excellent BBB permeability, robust labelling of A $\beta$  plaques in transgenic AD mouse brains, and compatibility with confocal laser scanning microscopy (CLSM) and FLIM for quantitative mapping of A $\beta$  burden across disease stages. Beyond tissue imaging, TZ-48 enables sensitive detection of A $\beta$  in CSF and blood serum, accurately distinguishing AD from healthy mice.

To facilitate clinical translation, the team of scientists consisting of Krithi K. Bhagavath, Madhu Ramesh, Yogendra Kumar, Sabyasachi Mandal, Hiriyakkanavar Ila and Thimmaiah Govindaraju developed ADxFluor, a smartphone-integrated platform leverages the fluorescence response of TZ-48 for rapid, unbiased quantification of serum A $\beta$  load.

The system combines dual-mode brain imaging, biofluid detection, and smartphone-based quantification of A $\beta$  in biofluids, establishing it along with ADxFluor, a smartphone-integrated platform as a foundation for next-generation smart diagnostics for AD and other neurodegenerative diseases.

The integration of TZ-48 with the smartphone-based ADxFluor platform further establishes a portable, low-cost, and user-friendly point-of-care diagnostic system, representing a significant technological and translational innovation in AD diagnostics.

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