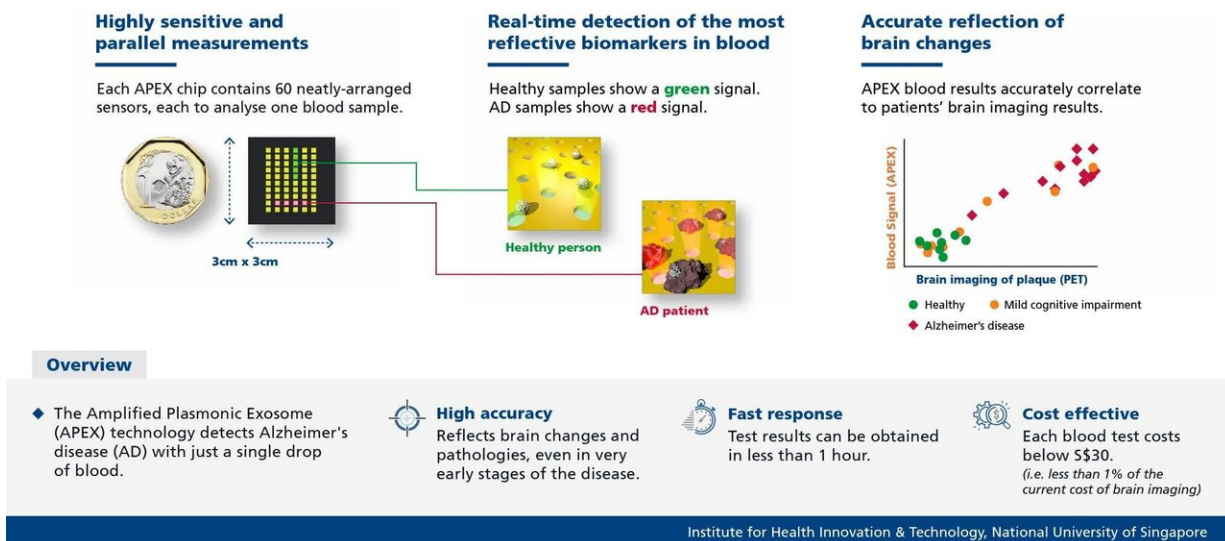


Researchers develop new blood test for faster, cheaper and more accurate detection of Alzheimer's disease

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Blood test for faster, cheaper and accurate detection of Alzheimer's disease

New APEX technology invented by NUS researchers



The APEX system could open doors to more effective detection of Alzheimer's disease. Credit: National University of Singapore

Doctors may one day be able to diagnose Alzheimer's disease (AD), the most common cause of severe dementia, and monitor a patient's response to treatment by doing a simple blood test. This is made possible

using the APEX (Amplified Plasmonic EXosome) system invented by researchers from the National University of Singapore (NUS).

Designed to pick up an early-stage molecular marker of AD, the aggregated amyloid beta (A β), the APEX system could potentially diagnose AD even before clinical symptoms appear.

This [novel technology](#) is highly sensitive and provides an accurate diagnosis—comparable to brain PET imaging, the current gold standard for AD diagnosis—at about S\$30 per test, which is less than one percent of the cost of PET imaging. The current design could test 60 samples simultaneously and results are available in less than one hour. As the APEX system uses native [blood](#) plasma without additional sample processing, it conducts direct measurement and is very simple to use in clinical settings.

Led by Assistant Professor Shao Huilin from the NUS Institute for Health Innovation & Technology (NUS iHealthtech), the 12-member research team spent two years developing APEX. The team recently published its research findings in prestigious scientific journal *Nature Communications*. The study was featured as an Editors' Choice by the journal.

Early detection and monitoring of AD

Dementia is the public health crisis of the 21st century. In 2018, dementia has affected 50 million people worldwide, and the number is expected to rise to 82 million by 2030 and 152 million by 2050. Every year, over 9.9 million new cases of dementia are diagnosed worldwide.

AD is the most common cause of dementia. Due to the complex and progressive nature of AD, early detection and intervention can improve the success of disease modifying therapies. Unfortunately, current AD

diagnosis and monitoring—using clinical evaluation and neuropsychological assessments—are subjective and the disease tends to be detected only at a late stage. Other alternatives such as PET imaging and cerebrospinal fluid test are either too expensive for wide clinical adoption or require invasive lumbar punctures.

Blood-based tests, on the other hand, have the advantage of being safe, affordable and easy to administer. However, one key challenge for scientists is that blood has very low concentrations of AD molecules, and not all of these molecules are disease-reflective, making detection and diagnosis very difficult.

The invention by the NUS team is therefore a big step forward by providing a solution to effectively 'capture' and measure the most meaningful AD molecules in blood samples and amplify them for analysis.

Asst Prof Shao said, "There is currently no good blood-based method to effectively screen and monitor AD. New tests that are under investigation have either poor accuracy or low sensitivity. The APEX technology addresses both of these limitations and is therefore a very powerful and objective companion diagnostic system to complement existing clinical and neuropsychological tests for early detection and better management of AD."

"As blood tests are relatively easy to administer, APEX can be also used to monitor a patient's response to treatment. Furthermore, this technology can be easily scaled up for large cohort clinical validations and drug evaluation," she added.

Innovative APEX technology

A key characteristic of AD is the buildup of [amyloid beta](#) (A β) proteins

in the brain. These A β proteins clump up as aggregates and kill brain cells. A β proteins are also released into, and circulate through, the bloodstream. The APEX system is uniquely designed to detect and analyse the earliest aggregated forms of A β proteins in blood samples, to enable detection of AD even before clinical symptoms appear and to accurately classify the disease stages.

"Traditional technologies measure all A β molecules found in the blood, regardless of their aggregation states, and thus show poor correlation to brain pathology. Our study found that the aggregated form of the protein could accurately reveal brain changes and reflect AD disease stages," said Ms Carine Lim, a doctoral student from NUS iHealthtech and NUS Department of Biomedical Engineering, and co-first author of the study.

The APEX technology is size-matched to distinguish this group of reflective A β proteins directly from blood samples. Each APEX chip is 3 cm by 3 cm—about a quarter the size of a credit card, and contains 60 neatly-arranged sensors, each to analyse one blood sample.

"Within each APEX sensor, there are millions of nanoholes to enable unique interactions with the aggregated A β . The APEX sensor recognises the abnormal A β aggregates directly from a very small amount of blood, induces and amplifies a colour change in the associated light signal," said Mr Zhang Yan, a doctoral student from NUS iHealthtech and NUS Department of Biomedical Engineering, and co-first author of the study.

Superior results from clinical study

To determine the performance of the APEX system, Asst Prof Shao and her team conducted a clinical study involving 84 individuals, including patients who have been diagnosed with AD or mild cognitive impairment (MCI), as well as a control group comprising healthy individuals and

patients diagnosed with vascular dementia or neurovascular compromises. PET imaging and blood sampling were conducted on all participants.

"The results of the APEX tests correlate extremely well with PET imaging results. The clinical study shows that the APEX system can accurately identify patients with AD and those with MCI; it also differentiates them from healthy individuals and patients suffering from other neurodegenerative diseases. In fact, this is the only blood test that shows such comparable results with PET imaging, the current gold standard for AD diagnosis," Asst Prof Shao explained.

Next steps

Asst Prof Shao and her team are currently in discussions with industry partners to commercialise this technology. The device is expected to reach market within the next 5 years.

In the next phase of research, the team hopes to employ the technology in areas of AD disease management as well as for evaluation of AD therapeutics under development.

More information: Carine Z. J. Lim et al. Subtyping of circulating exosome-bound amyloid β reflects brain plaque deposition, *Nature Communications* (2019). [DOI: 10.1038/s41467-019-09030-2](https://doi.org/10.1038/s41467-019-09030-2)

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