NEWS RELEASE

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NTU Singapore scientists invent a coin-sized device to rapidly isolate blood plasma for diagnostics and precision medicine

Scientists at **Nanyang Technological University, Singapore (NTU Singapore)**, have developed a coin-sized chip that can directly isolate blood plasma from a tube of blood in just 30 minutes, which is more convenient and user-friendly as compared to the current gold standard, multi-step centrifugation process.

Named **ExoArc**, in just one step, it can achieve high blood plasma purity by removing more than 99.9 per cent of blood cells and platelets precisely and gently.

This will greatly speed up clinical analysis of the cell-free DNA and RNA molecules, as well as nanoparticles commonly known as extracellular vesicles. These particles are often used to screen for biomarkers that are tell-tale signs specific to certain cancers and diseases.

Currently, the only way to isolate blood plasma is through using a centrifuge, which spins blood samples at high speeds, separating the blood cells from the plasma.

However, even after two rounds of spinning in the centrifuge, there will still be some cells and platelets present in the blood plasma which can break down or degrade, releasing additional bio-content, thus leading to unwanted materials that affect the accuracy of diagnostic tests.

As a proof-of-concept, the team built a portable prototype device (measuring 30cm x 20cm x 30cm) to house the ExoArc chip (3.5cm x 2.5cm x 0.3cm), which has a large touch-screen interface to adjust settings, as well as internal pumps and pipings for the processing of blood samples and collection of the isolated blood plasma.

Together with clinician-scientists from **National Cancer Centre Singapore (NCCS)**, **Tan Tock Seng Hospital (TTSH)**, and the **Agency for Science, Technology and Research (A*STAR),** the team clinically validated ExoArc by analysing the microRNA profile of blood plasma in healthy people and cancer patients using a biomarker panel

and found it was able to diagnose non-small cell lung cancer with a sensitivity of 90 per cent.

As an innovation, ExoArc currently has two patent applications filed through **NTUitive**, NTU's innovation and enterprise company and its study findings have been published recently in *ACS Nano*[1], a journal under the *American Chemical Society*.

Lead scientist of the study, NTU **Associate Professor Hou Han Wei**, said the team aimed to find a quicker solution that could replace the centrifuge, while still yielding high-quality plasma for disease screening and research.

"It has been nearly 160 years since the invention of the first centrifuge and about 50 years since modern high-speed centrifuges became a standard tool in laboratories [2] for preparing blood samples. Despite these advancements, separating complex liquids like blood, which comprises various cell types and a diverse range of biological materials, remains a challenge," explained Assoc Prof Hou, a biomedical engineer from the **School of Mechanical and Aerospace Engineering** and **Lee Kong Chian School of Medicine (LKCMedicine)**.

"By leveraging unique flow phenomenon in tiny channels in a chip that is about the size of a dollar coin, we can now efficiently separate small biological materials based on their size without using any physical membrane or filters. We have transformed this breakthrough technology into a device about size of a small desktop printer, featuring disposable plastic chips to prevent cross-contamination in clinical testing."

Co-author of the paper, **Professor Darren Lim, Senior Consultant in the Division of Medical Oncology at NCCS and Director of Research at the SingHealth Duke-NUS Lung Centre**, explained the importance of high-quality blood plasma.

"Reducing contamination from degraded blood cells is crucial for the accuracy of diagnostic tests. Our study shows that this device allows quicker and more precise clinical diagnoses, significantly decreasing the waiting time for test results, reducing patients' anxiety and ultimately improving their overall care. This is particularly significant for cancer treatment," said Prof Lim.

In another demonstration of its broad application, the team used ExoArc to study microRNA molecules from blood plasma samples from healthy individuals and those with type 2 diabetes mellitus using quantitative polymerase chain reaction (PCR).

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[1] *ACS Nano 2024, 18, 8, 6623–6637, Publication Date: February 13, 2024, https://doi.org/10.1021/acsnano.3c12862*

[2] *Marshall Scientific. (n.d.). The history of the centrifuge. Retrieved from https://www.marshallscientific.com/the_history_of_the_centrifuge_a/349.htm*

From just one tube of blood, they identified 293 different microRNA molecules. The research team also found that the microRNA profile from plasmas and extracellular vesicles from individuals with type 2 diabetes had a different composition as compared to healthy participants. This suggests the potential of ExoArc in helping to isolate and identify disease-related biomarkers.

Associate Professor Rinkoo Dalan, **Senior Consultant** specialising in diabetes and endocrinology at **Tan Tock Seng Hospital**, said the initial results are promising and show the potential of ExoArc being able to help drive precision medicine.

“This technology can help clinicians better predict and manage complications of chronic metabolic conditions like diabetes, by providing more accurate, timely, and individualised information. By detecting specific biomarkers accurately, we can tailor treatments to the unique needs of each patient, potentially improving outcomes and enhancing the quality of care,” said Assoc Prof Dalan, who is also a teaching faculty at LKCmedicine.

ExoArc vs conventional centrifuge

The current gold-standard method of isolating blood plasma relies on centrifuges, which is not foolproof and is highly dependent on the skill of the technicians who manually extract the plasma after each spin.

Even after two centrifugation rounds, which can take up to an hour, residual biological cells can remain in the plasma, potentially contaminating RNA tests and leading to inaccurate results.

One of the key reasons is that blood tests are time-sensitive, requiring processing within a day or even a few hours to prevent the rapid degradation of biological material from cells. This breakdown introduces additional DNA, RNA or vesicles into the plasma, which can distort test outcomes.

Laboratories typically wait to accumulate multiple blood samples before using the centrifuge, extending the isolation process by several hours. This delay combined with the extended duration of centrifugation and operator variability, sometimes makes it challenging to compare scientific findings between different research labs.

Unlike the centrifuge machine which usually process multiple tubes of blood samples, ExoArc technology can be scaled up by designing multiple channels to simultaneously isolate blood plasma as and when blood samples are received in clinics or hospitals in a faster and more consistent manner.

In future, this process could be automated into a one-step process, which would significantly reduce the time needed to prepare samples for testing and will streamline

the diagnostic process, potentially helping to reduce overall cost. By adjusting the size-cutoff, this platform technology can also be used to isolate bacteria or viruses from blood or other biofluids.

The development of ExoArc is backed by a Proof-of-Concept and Proof-of-Value grant from the NTUitive Gap Fund, under the NTU Innovation and Entrepreneurship initiative. This initiative seeks to turn research into practical innovations that address societal challenges, like an ageing population, and generate significant economic benefits for Singapore.

The study also included contributions from scientists at the Massachusetts Institute of Technology and the University of Texas Medical Branch (Galveston).

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Notes to Editor:

Paper titled: "High-Throughput Microfluidic Extraction of Platelet-free Plasma for MicroRNA and Extracellular Vesicle Analysis", published in ACS Nano, 13 Feb 2024. https://doi.org/10.1021/acsnano.3c12862

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About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,000 undergraduate and postgraduate students in the Engineering, Business, Science, Medicine, Humanities, Arts, & Social Sciences, and Graduate colleges.

NTU is also home to world-renowned autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Earth Observatory of Singapore, Nanyang Environment & Water Research Institute and Energy Research Institute @ NTU (ERI@N).

Under the NTU Smart Campus vision, the University harnesses the power of digital technology and tech-enabled solutions to support better learning and living experiences, the discovery of new knowledge, and the sustainability of resources.

Ranked amongst the world's top universities, the University's main campus is also frequently listed among the world's most beautiful. Known for its sustainability, NTU has achieved 100% Green Mark Platinum certification for all its eligible building projects. Apart from its main campus, NTU also has a medical campus in Novena, Singapore's healthcare district.

For more information, visit www.ntu.edu.sg