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PRESS RELEASE

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NUS scientists a step closer to developing blood test to monitor status of cancer and treatment outcome

New technique efficiently captures and grows tumour cells to guide selection of drug therapy

Singapore, 24 November 2015 – Scientists from the National University of Singapore (NUS) have developed a novel technique to efficiently culture clusters containing circulating tumour cells (CTCs) in 14 days that could be used to predict the outcome of cancer treatment as well as monitor the status of cancer. Using the technique, the team achieved a success rate of more than 60 per cent in culturing CTCs from patients with metastatic breast cancer, the highest known success record to-date. This breakthrough brings researchers a step closer towards enabling personalised cancer treatment and monitoring.

The study was conducted by scientists from the Mechanobiology Institute (MBI) and Cancer Science Institute of Singapore (CSI) at NUS and in collaboration with the National University Cancer Institute, Singapore (NCIS). A paper describing the work was published earlier in the medical journal *Oncotarget*.

Professor Lim Chwee Teck, who is from MBI and one of the lead authors, explained, "Being able to capture CTCs and grow them efficiently from a blood sample is a big step forward in liquid biopsy for tumour diagnosis and cancer treatment monitoring. This could potentially mean that biopsy for cancer diagnosis and prognosis could be done using a blood test, which is minimally invasive, instead of having to remove cells from the tumour itself. Results of the blood tests could help doctors assess the best therapy options for a patient, and frequent blood tests can also be done during the course of an anti-cancer treatment to monitor a patient's progress during treatment."

Tests can potentially be done on the cultured CTCs to guide the selection of drug therapy, added Adjunct Associate Professor Lee Soo Chin, Associate Director (Research) and Senior Consultant of NCIS, who is also a Senior Principal Investigator from CSI, and the clinical lead for the study. "Cultured CTCs of individual patients can be tested for drug sensitivity to determine the responsiveness of the CTCs to the drugs that are commonly used in the

treatment of cancers. This could allow doctors to decide on the most suitable drug for the patient based on the drug sensitivity results. As the CTCs can be cultured in a short time period, the entire testing process can take as short as four weeks – two weeks for culturing the CTCs and two weeks for drug screening. Patients will not have to wait a long time for the test results."

Role of CTCs in cancer prognosis

Cancer is among the leading causes of death in Singapore today. More than a hundred types of cancers have been identified, each with distinct characteristics and treatment challenges. However, a major challenge in cancer management and treatment lies in its early detection and treatment, before the disease aggressively spreads to other parts of the body.

Cancer develops as a result of genetic anomalies which cause healthy cells to become cancerous and divide uncontrollably into a mass of abnormal cells, also known as tumours. Cancer metastases or spreads when cells gain the ability to escape from the primary tumour, circulate in the bloodstream, and a few cells eventually invade into other parts of the body to establish secondary tumours. These 'runaway' cells are called CTCs and they can be found even at early stages of the disease.

The team has been able to obtain cultures from screening of samples from some early-stage breast cancer patients. Hence, analysing patients' blood for CTCs may have potential applications in predicting patient progression or response to cancer treatment.

Said Adj Assoc Prof Lee, "Half of these early-stage breast cancer patients have been found to have CTCs in the culture after surgery and post-operative chemotherapy, despite them not having cancer that can be detected using conventional means such as scans and who are presumed cured. We will need to continue tracking these patients to determine if the persistence of these CTCs is associated with early cancer relapse."

Capturing and growing CTCs efficiently

CTCs comprise many sub-populations and occur at extremely low frequencies in blood. According to Prof Lim, "The chance of getting CTCs in a blood sample is akin to trying to find a hundred people in a world of seven billion people."

Owing to this rarity, the population of CTCs needs to be expanded before they can be used for clinical analysis. Currently, most methods used to culture CTCs have either lacked efficiency or required pre-selection techniques for the elimination of non-cancerous cells that led to the loss of some CTCs in the process.

In an attempt to overcome these setbacks, NUS scientists developed a novel methodology to efficiently culture clusters containing CTCs from blood samples. They created an ideal environment – using a combination of specially designed microwells and oxygen-deficient growth conditions – for tumour cells to grow while other non-cancerous cells gradually undergo cell death.

Tests were conducted on 226 clinical blood samples obtained from 92 metastatic or early-stage breast cancer patients who began anti-cancer therapy, and a success rate of over 60 per cent in culturing clusters containing CTCs was achieved using the novel technique, more than two to three times higher than conventional methods of culturing CTCs.

The team is also currently developing new technologies for liquid biopsies that will allow them to perform single cell analysis, so that each and every cell taken from the biopsy can be examined closely to obtain critical information that will be useful to scientists and clinicians to better treat the disease. Liquid biopsy, at present, is used to do a number count of CTCs to correlate with the severity of the cancer and track treatment outcomes.

Said Prof Lim, "Looking forward, my team and I will be embarking on research to develop novel technologies that can contribute towards personalised or precision medicine. Cancer is extremely difficult to treat due to presence of many sub-varieties of cancer cells, which may also further mutate and change. The genetic makeup and immune response of each individual can also result in very different outcomes despite receiving the same treatment. "One size fits all" approach has proven to be ineffective and only individual patient-derived information can help us do a better job. We are looking at developing technologies that can acquire such critical information so that clinicians can tailor and administer precise treatment for each individual patient."

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About National University of Singapore (NUS)

A leading global university centred in Asia, the National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education and research, with a focus on Asian perspectives and expertise.

NUS has 16 faculties and schools across three campuses. Its transformative education includes a broad-based curriculum underscored by multi-disciplinary

courses and cross-faculty enrichment. Over 38,000 students from 100 countries enrich the community with their diverse social and cultural perspectives.

NUS has three Research Centres of Excellence (RCE) and 26 university-level research institutes and centres. It is also a partner in Singapore's fifth RCE. NUS shares a close affiliation with 16 national-level research institutes and centres. Research activities are strategic and robust, and NUS is well-known for its research strengths in engineering, life sciences and biomedicine, social sciences and natural sciences. It also strives to create a supportive and innovative environment to promote creative enterprise within its community.

This year, NUS celebrates its 110th year of founding together with Singapore's 50th year of independence. As the island's first higher education institution established by the local community, NUS prides itself in nurturing generations of leaders and luminaries in Singapore and Asia.

For more information on NUS, please visit www.nus.edu.sg. Details on NUS' 110th Anniversary celebrations are available at nus110.sg.

About the National University Cancer Institute, Singapore (NCIS)

The National University Cancer Institute, Singapore (NCIS), a national specialty centre, offers a broad spectrum of cancer care and management covering both paediatric and adult cancers, with expertise in prevention, screening, diagnosis, treatment, rehabilitation and palliative care. The Institute adopts a multi-disciplinary approach to develop a comprehensive and personalised plan for each cancer patient and his or her family. NCIS draws on the expertise of its specialists in the fields of haematology-oncology, radiation oncology, gynaecologic oncology, paediatric oncology, surgical oncology, oncology nursing, oncology pharmacy, palliative care, pathology, radiology, medical specialties including gastroenterology and hepatology, infectious diseases, pulmonary and critical care, psychiatry, epidemiology and public health as well as other allied health sciences.

NCIS, which is part of the National University Health System (NUHS), is home to the Cancer Therapeutics Research Group, one of the few academic early phase cancer clinical trial groups spanning leading academic centers in Singapore, Hong Kong, Korea, Australia, and Taiwan. Its strength in research allows patients to access drugs and devices before they are commercially available. NCIS is also closely affiliated with the Cancer Science Institute of Singapore, National University of Singapore.

For more information about NCIS, visit www.ncis.com.sg