

MEDIA RELEASE

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AI PLATFORM PERSONALISES DRUG COMBINATIONS TO TREAT RELAPSED LYMPHOMA

New study shows effectiveness of QPOP-guided treatments for patients whose cancers grow despite standard therapy

Singapore — A new study published in October by experts in Singapore suggests that an artificial intelligence (AI) platform that identifies patient-specific drug combinations can help those whose lymphomas have relapsed.

The paper, published in the prestigious journal *Science Translational Medicine* on 19 October, is the first study demonstrating the feasibility of personalised drug combination prediction for patients with lymphoma, and utilises a novel method called quadratic phenotypic optimisation platform (QPOP) that is developed in the National University of Singapore (NUS).

The method involves collecting a small tumour sample from a patient and incubating this in a laboratory with a set of 12 carefully selected drugs used for lymphoma. After 72 hours, QPOP then ranks the patient's cancer cells' potential response to more than 750 distinct drug combinations of up to four drugs, using these 12 possible drugs.

This clinical application study of QPOP, the first-of-its-kind, was a collaboration between clinicians at the National University Cancer Institute, Singapore (NCIS) and scientists from the Cancer Science Institute of Singapore (CSI Singapore) at NUS.

Previous studies have focused only on predicting the sensitivity of single drugs for treatment due to limitations on the amount of tissue available from biopsies. The automated workflow and AI methods in QPOP allowed the researchers to use even a small amount of tissue from biopsies to study combination drug sensitivities.

Lymphoma (lymphoid neoplasm) is the fifth most common cancer in Singapore, according to figures from the Singapore Cancer Registry Annual Report 2019.

Dr Anand Jeyasekharan, lead investigator of the study and Consultant at the Department of Haematology-Oncology, NCIS, said lymphoma is typically treated with chemotherapy combinations, but about four in 10 patients with aggressive lymphomas may not eventually respond to standard medications or suffer from a relapse.

When this happens, treatment options are limited. By the time patients reach third-line treatment, their chance of success in responding to standard chemotherapy combinations is only about 10 per cent.

The study showed that 65 out of 71 patients enrolled had a successful QPOP test, with identification of patient-specific combinations within a week of the biopsy. Among those patients whose lymphomas were resistant to standard therapy, 17 went on to receive QPOP-guided treatments based on prior clinical evidence and physician discretion.

Among these 17 patients, five achieved a complete response to treatment, such that they had no more signs of cancer. Three patients achieved a partial response and the remaining nine had stable disease or progressive disease.

The researchers noted that “it was unusual to see these complete and partial responses to unique combinations in patients who would otherwise have had no effective standard treatment options”.

The researchers also reported reduced time to disease progression after QPOP-guided treatments, especially in patients who received three or more lines of treatment. In comparison with their previous standard treatments, QPOP-guided treatments more than doubled a patient’s progression-free survival, or length of time that the cancer does not grow or spread further.

The patients were recruited through NCIS and its clinical collaborators at the National Cancer Centre Singapore and Singapore General Hospital from November 2017 to August 2021.

Dr Jeyasekharan, who is also Principal Investigator at CSI Singapore, said: “Most relapsed cancers are not curable, but with advances in research, the aim is to convert cancer into a chronic disease that people can live with – similar to diabetes or hypertension. However, currently approved cancer drugs work only for a subset of patients, due to wide variability within molecular features of cancers even within a single subtype. In patients where standard treatments fail, there is an urgent need to identify better strategies to improve their outcomes.”

Dr Jeyasekharan estimated that in a year, up to 200 patients in Singapore with relapsed lymphoma can potentially benefit from QPOP, which could help doctors make personalised clinical decisions in treating their cancer. As at November 2022, 160 patients had enrolled in the QPOP study at NCIS/CSI Singapore, and the team intend to move this into a formal clinical trial moving forward.

Associate Professor Edward Chow, Principal Investigator at CSI Singapore and the lead scientific researcher who led the development of QPOP, said: “The individualised treatment offered through QPOP is a departure from the traditional approach where doctors follow standard protocols based on the subtype of cancer. QPOP can quickly derive a likely effective treatment for the patient without having to subject him or her to the actual physical burden of the drugs, saving precious time and resources.

“We know that cancer is very difficult to treat, so we hope to at least prolong survival time and make cancer patients’ lives a little better,” he added.

The researchers believe QPOP can ultimately be applied to all types of cancer, but this will depend on advances in culturing cancer cells and tumour tissues in the laboratory. Instead of harnessing QPOP only after standard treatments have failed, they hope to eventually use the technology at earlier stages of treatment so it could potentially lower costs for patients.

The preclinical and clinical studies for QPOP were supported by the Singapore Ministry of Health's National Medical Research Council, Ministry of Education and the National Research Foundation, Singapore¹.

Patient profile

Madam Peggy Tay, a 73-year-old retired administrator, is one of the 17 patients in the study published in international journal *Science Translational Medicine*. She has benefited from the application of QPOP to devise her treatment plan. Madam Tay was first diagnosed with Diffuse Large B-cell Lymphoma, an aggressive type of blood cancer, in May 2012. She underwent chemoimmunotherapy with a good response, but suffered a relapse in January 2019. After a brief response to salvage chemotherapy, a standard treatment for relapsed lymphoma, her disease relapsed again in September 2019.

When QPOP analysis was performed, the results revealed that her cancer had a strong sensitivity to a combination of palbociclib and everolimus medication, which had previously been tested only in breast cancer.

After having no response to a standard anti-cancer treatment, she was started on the palbociclib-everolimus combination treatment in December 2019. She started feeling better almost immediately and had a complete response to the treatment. Today, she is doing well and continues to be in remission. She has resumed her hobby of painting and has given her oncologist, Dr Anand Jeyasekharan, one of her artworks.

Chinese Glossary

National University Cancer Institute, Singapore (NCIS)	新加坡国立大学癌症中心 (国大癌症中心)
Cancer Science Institute of Singapore (CSI Singapore)	新加坡癌症科学研究所
National University of Singapore	新加坡国立大学
National Medical Research Council (NMRC)	全国医学研究理事会
Dr Anand Jeyasekharan Consultant Department of Haematology-Oncology, NCIS Principal Investigator CSI Singapore	阿南德顾问医生 肿瘤血液科, 新加坡国立大学癌症中心 (国大癌症中心) 新加坡癌症科学研究所主要研究员

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Quadratic phenotypic optimisation platform (QPOP)	二次表型优化平台

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About National University Cancer Institute, Singapore (NCIS)

The National University Cancer Institute, Singapore (NCIS) is a national specialist centre under the National University Health System (NUHS), and is the only public cancer centre in Singapore that treats both paediatric and adult cancers in one facility. NCIS (*n-sis*) offers a broad spectrum of cancer care and management from screening, diagnosis and treatment, to rehabilitation, palliative and long-term care. NCIS's strength lies in the multidisciplinary approach taken by our clinician-scientists and clinician-investigators to develop a comprehensive and personalised plan for each cancer patient.

NCIS cancer services span across several acute hospitals: NCIS @ National University Hospital, NCIS @ Ng Teng Fong General Hospital, NCIS @ Alexandra Hospital, and the NCIS Radiation Therapy Centre @ Tan Tock Seng Hospital. We also deliver a range of cancer services for our patients' convenience at satellite clinics in the community, as well as in the comfort of their homes. For more information, please visit www.ncis.com.sg.

About the Cancer Science Institute of Singapore (CSI Singapore)

The Cancer Science Institute of Singapore (CSI) is one of only six Research Centres of Excellence established by the Government of Singapore with funding from the National Research Foundation and the Ministry of Education. Its mission is to better understand the causes of human cancer across Asia, and thereby improve its detection, treatment and prevention for the benefit of the patients. The CSI's outstanding researchers and excellent scientific facilities create an energetic environment for ground-breaking research and world-class training. The CSI is internationally recognized for its innovative research on the biology of cancers prevalent in Asia, and for taking new methods for cancer treatment from the



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laboratory to the clinic. Through its local and global partnerships, the CSI works with leading minds from multiple scientific and clinical disciplines in Singapore, the USA and Europe, both in academia and in industry.

For more information on CSI Singapore, visit <https://www.csi.nus.edu.sg/web/>.