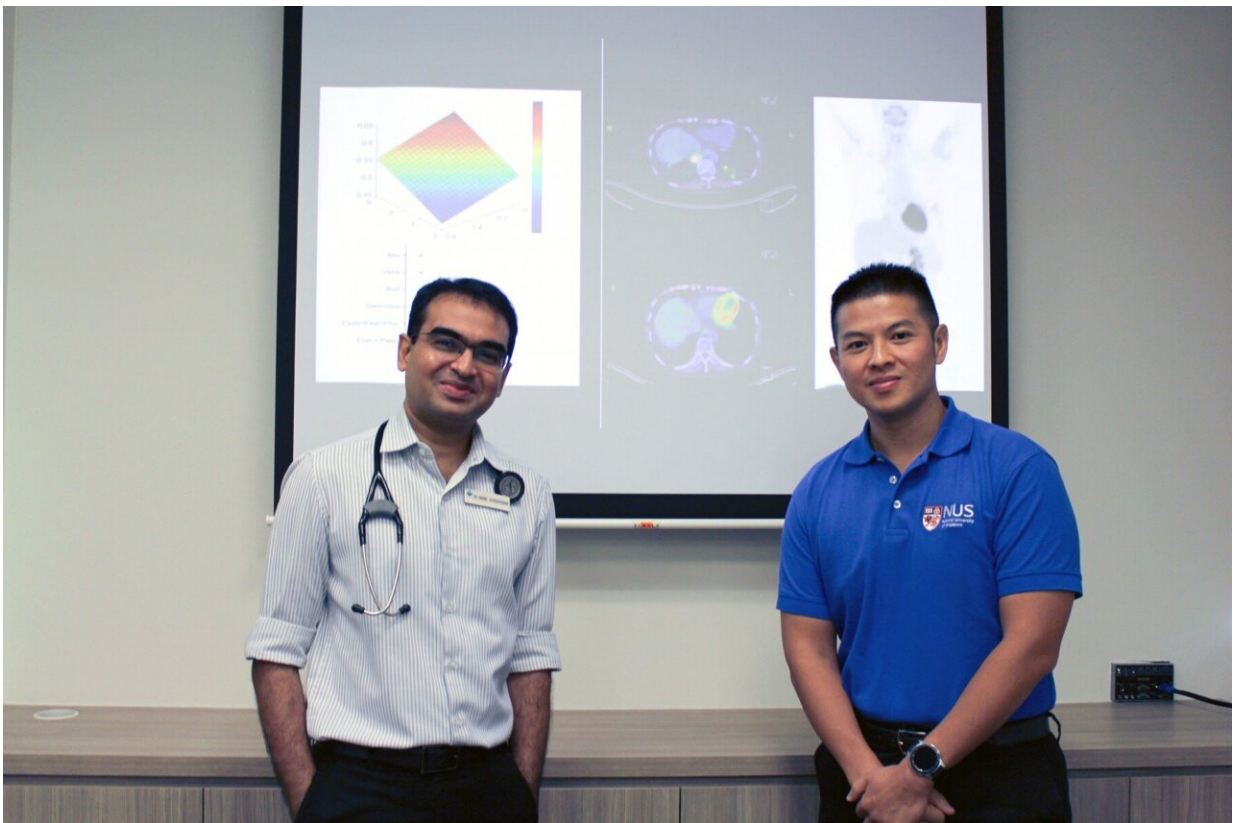


AI-guided personalized drug combinations to treat relapsed lymphoma

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Asst Prof Anand Jeyasekharan (left) and Assoc Prof Edward Chow (right) from the Cancer Science Institute of Singapore at NUS are pioneering the application of QPOP, an AI-platform developed by NUS researchers to identify patient-specific drug combinations, for the treatment of cancer. Credit: National University of Singapore

A new study published 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 journal *Science Translational Medicine* on October 19, is the first study demonstrating the feasibility of personalized [drug](#) combination prediction for patients with lymphoma, and utilizes a novel method called QPOP (quadratic phenotypic optimization platform) that is developed in the National University of Singapore (NUS).

The method involves collecting a small tumor 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.

Benefitting patients with relapsed lymphoma

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

Assistant Professor Anand Jeyasekharan, lead investigator of the study and Consultant at the Department of Hematology-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%.

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 treatment, 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 Center Singapore and Singapore General Hospital from November 2017 to August 2021.

Individualized treatments to improve patient outcomes

Asst Prof 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."

Asst Prof 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 personalized 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 individualized 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 tumor 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](#).

More information: Jasmine Goh et al, An ex vivo platform to guide drug combination treatment in relapsed/refractory lymphoma, *Science Translational Medicine* (2022). [DOI: 10.1126/scitranslmed.abn7824](https://doi.org/10.1126/scitranslmed.abn7824)

Provided by National University of Singapore

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