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Study findings support the use of a personalised medicine approach to treat Soft Tissue Sarcomas

- ***Researchers used precision medicine platform, Quadratic Phenotypic Optimisation Platform (QPOP), to predict treatment response and identify effective drug combinations for soft tissue sarcomas (STS).***
- ***Results highlight a promising drug pairing of AZD5153 and pazopanib to treat STS.***
- ***Findings support the potential of using data-driven, phenotypic screening in guiding personalised cancer therapies for STS.***

SINGAPORE – A study conducted by researchers from the Agency for Science, Technology and Research (A*STAR), National Cancer Centre Singapore (NCCS) and National University of Singapore (NUS), in collaboration with biotech company, KYAN Technologies, has demonstrated that a precision medicine approach improves treatment selection for patients with soft tissue sarcomas (STS) in a clinical setting. Published in *npj Precision Oncology* in March 2025, the study's findings support using data-driven and phenotypic screening approaches to treat STS.

STS are rare, heterogeneous tumours that account for less than 1% of all cancers globally. However, they disproportionately represent a significant portion (20%) of paediatric and young adult malignancies, affecting individuals in the prime of their lives. The challenge in treating STS is that conventional chemotherapy often yields unpredictable and poor results. As the biological diversity of these tumours and their rarity have made conducting large-scale clinical trials difficult, researchers postulated that the best way to target STS would be through a precision medicine approach, analysing each patient's unique tumour characteristics to potentially improve response rates and reduce toxicities.

The research team utilised the Quadratic Phenotypic Optimisation Platform (QPOP) to apply precision medicine approaches to treat STS. QPOP uses data-driven, phenotypic screening to identify effective cancer treatment combinations from a panel of approved drugs and investigational treatments, with a turnaround time of 7 days. The team:

1. Analysed if QPOP was clinically accurate in predicting drug sensitivity by screening the tumour samples of 45 primary STS patients – the largest reported *ex vivo* drug

testing cohort to date. Results showed over 70% of patient responses to standard of care treatments matched with results from *ex vivo* testing in QPOP, validating the accuracy and reliability of the platform.

2. Identified unconventional personalised drug combinations through QPOP for a subset of STS patients unresponsive to standard treatments. These targeted approaches were used to select treatments for two patients who had compelling clinical responses. This application underscores the potential of functional precision medicine to identify alternative treatment strategies for complex and treatment-resistant STS.
3. Explored the use of QPOP to identify new treatment combinations for STS, thereby discovering that the combination of AZD5153 (a BRD4 inhibitor) and pazopanib (a multi-kinase blocker) is more effective than standard treatment across multiple STS subtypes. This was further validated in the lab in patient-derived cell lines and *in vivo* models. The combination therapy effectively repressed MYC, a well-known oncogene that is difficult to target, and other related pathways that play critical roles in STS and various other cancers.

The study was led by Assistant Professor Valerie Yang, Visiting Consultant in the Division of Medical Oncology at the National Cancer Centre Singapore (NCCS) and Joint Research Clinician and Group Leader at the A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB), with co-corresponding authors from NUS, Dr Tan Boon Toh and Dr Edward Kai-Hua Chow, with bioinformatics expertise contributed by Dr Xing Yi Woo of A*STAR Bioinformatics Institute.

“This work is game-changing for several reasons. We show that *ex vivo* drug testing of patient-derived cells in these rare cancers can not only accurately predict patient responses to drugs but can also provide important information to derive good disease control in selected cases in patients who have exhausted all treatment options. What is also exciting is the novel drug combination that was identified may supersede existing treatment for soft tissue sarcomas,” said Asst Prof Yang.

“This study marks a pivotal step toward transforming how we treat rare and aggressive cancers like soft tissue sarcomas. By leveraging QPOP to match patients with optimised drug combinations based on their tumor biology, we move closer to realising the promise of functional precision medicine — offering real hope for better outcomes where conventional therapies have fallen short,” said Dr Toh, Head of the Translational Core Laboratory at the N.1 Institute for Health at NUS and Senior Research Fellow at the Institute for Digital Medicine (WisDM) at the NUS Yong Loo Lin School of Medicine.

Further clinical trials are needed to confirm these results and to explore the broader applicability of QPOP in other cancer types. The team are currently planning to run a prospective clinical trial in Singapore.

Study citation: Chan, S.P.Y., Rashid, M.B.M.A., Lim, J.J. et al. Functional combinatorial precision medicine for predicting and optimising soft tissue sarcoma treatments. npj Precis. Onc. 9, 83 (2025). <https://doi.org/10.1038/s41698-025-00851-7>

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About A*STAR Bioinformatics Institute (A*STAR BII)

The A*STAR Bioinformatics Institute (BII) is dedicated to computational biology/bioinformatics driven life science research aimed at the discovery of biomolecular mechanisms guiding biological phenomena. The final goals are scientific advancement leading to economic and societal impact for Singapore. BII covers everything from enterprise-grade secure clinical data hosting to state-of-the-art analysis and new method

development. Sophisticated theoretical and computational approaches including artificial intelligence are applied to analyze biological and clinical omics data (biomolecular sequences, expression profiles, epigenetics data), 3D structures of macromolecules and biological as well as medical cellular, tissue and macroscopic images from local and international academic, hospital and industry collaborators, public resources and from own experiments. Applied research diversifies into infectious diseases, digital pathology, precision medicine, cancer research, drug discovery, etc. Our vision is: "We add value to biomedical data". For more information on BII, please visit www.a-star.edu.sg/bii

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The National Cancer Centre Singapore (NCCS) is a leading national and regional tertiary cancer centre with specialists who are experts in treating cancer. In addition to offering holistic and multidisciplinary oncology care, our clinicians and scientists collaborate with local and international partners to conduct robust, cutting-edge clinical and translational research. To achieve its vision of being a global leading cancer centre, NCCS offers world-class care and shares its depth of experience and expertise by training local and overseas medical professionals.

To meet growing healthcare needs, the new NCCS building opened in 2023 with increased capacity and expanded facilities dedicated to cancer care, rehabilitation, research and education. To give patients the best treatment outcomes, advanced and innovative treatment such as proton therapy is offered at the new Goh Cheng Liang Proton Therapy Centre at NCCS.

About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore,

with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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