SINGAPORE SCIENTISTS DEVELOP MACHINE-LEARNING MODEL TO ANALYSE CANCER CELLS TO IMPROVE TREATMENT



A collaboration between two teams, led by Drs Niranjan Nagarajan and Ramanuj DasGupta, in A*STAR's Genome Institute of Singapore (GIS) developed a machine-learning model – <u>CaDRReS-Sc</u> – that analyses the relationship between cancer cell types and their drug sensitivity levels for recommending mono and combinatorial therapies. The research was published on *Genome Medicine* on 16 December 2021.

Tumours comprise populations of malignant cells that display phenotypic heterogeneity such as different growth rates and drug sensitivity levels. Cancer cell types with different genomic backgrounds tend to respond to the same drug differently. Researchers therefore analyse genomic information across cells types to understand intra-tumour heterogeneity and facilitate cancer treatment.

> "Tumours comprise a mixture of heterogeneous cells or cell populations, each with its preferential drug sensitivity for different anti-cancer drugs. Harnessing the power of single cell genomics helps us identify gene expression signatures, at the resolution of individual cells or clones of cells, that predict their therapeutic vulnerabilities, thereby enabling the discovery of novel, combinatorial therapies that can target the different subpopulations within a heterogeneous tumour."

> > Dr Ramanuj DasGupta, Senior Group Leader, Laboratory of Precision Oncology and Cancer Evolution, GIS, and corresponding author of the study

While traditional DNA/RNA sequencing technologies only allow measuring molecular properties of a tumour as a whole, recent sequencing technologies enable measurement at the single-cell level. In this research, the teams developed an intelligent machine-learning model (CaDRReS-Sc) that can predict which types of cells are sensitive to which type(s) of anti-cancer drug. The model considers intra-tumour heterogeneity to recommend a combination of



drugs to inhibit multiple cancer cell types within a tumour.



"It is well known that tumours comprise populations of malignant cells that have varying sensitivity to anti-cancer drugs. Advances in sequencing technologies have enabled studies into intra-tumour heterogeneity at the single-cell level. There is a need to apply machine-learning techniques that carefully take into account intratumour heterogeneity to recommend mono and combinatorial therapies, as well as facilitate drug-repurposing studies to improve cancer treatment."

Dr Niranjan Nagarajan, Associate Director, Laboratory of Metagenomic Technologies and Microbial Systems, GIS, and corresponding author of the study

"Cancer drug response prediction has been a crowded area for several years. Most existing studies focus on advanced modeling techniques that use existing data in their original form. In contrast, GIS' research focuses not only on techniques to process existing and newly generated data, but also on designing a new computational model for higher accuracy of drug response prediction in the presence of intra-tumour heterogeneity."



