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NOVEL TECHNOLOGY TO INVESTIGATE GENE ACTIVITIES AND MUTATIONS IN CANCER CELLS

Knowing how mutations in cancer cells work will help researchers better understand how they evolve to become resistant to drugs

Singapore – Scientists from Agency for Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS), the National Cancer Centre Singapore (NCCS) and Fluidigm Corporation have developed a new technology to simultaneously and systematically investigate individual cancer cells within a tumour. The study was published in [Clinical Chemistry](#) on 7 December 2018.

It has been established that not every cancer cell in a tumour is alike (also known as clonal heterogeneity), and that mutations develop in the cells during the course of tumour growth. Some of these mutations can cause the tumour to evolve and develop resistance against therapy. To understand the complexity of this process, it is therefore often necessary to sequence the entire tumour.

However, there are limitations to existing technologies that illuminate the different components of a tumour, and how such mutations change its characteristics. In particular, it is technically challenging to simultaneously sequence a single cell's DNA and analyse the activities of genes.

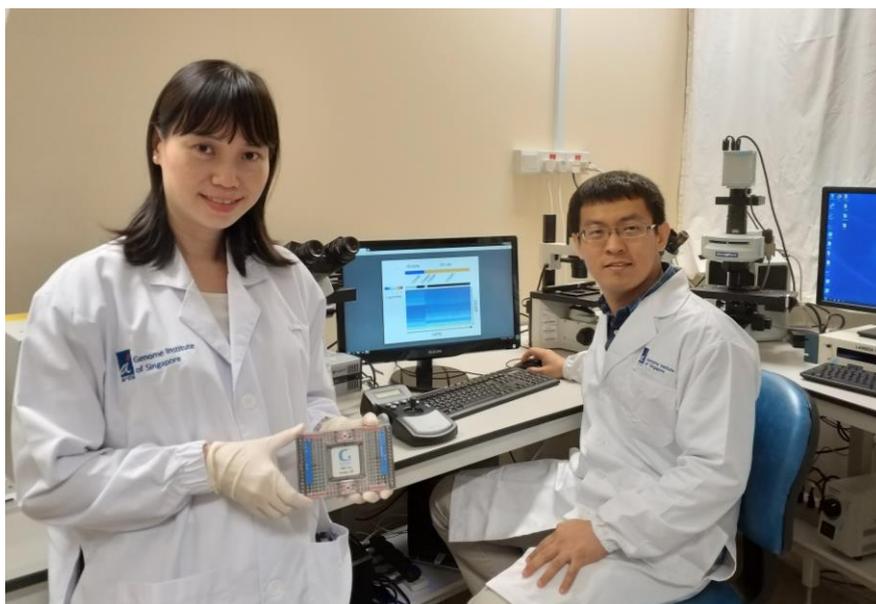
To address this problem, the team headed by Dr Axel Hillmer, Group Leader at GIS and senior author of this study, developed a novel technology termed **CO**ncurrent single cell **R**NAs and **T**argeted **D**NAs sequencing (CORTAD-seq) – on an automated Fluidigm C1 microfluidic platform. CORTAD-seq allows researchers to test for the presence of mutations in single cells with high accuracy and take snapshots of the gene activities within those cells.

Dr Kong Say Li, Research Associate at GIS and lead author of this study, said, "CORTAD-seq is a tool which can be implemented easily by other researchers, and lead to more impactful discoveries. This method allows for insights into cancer evolution and clonal heterogeneity, the mechanisms of drug resistance towards targeted therapy, as well as the difference in gene activities of cancer and normal cells through the identification of cancer mutations."

Dr Mark Lynch, Director of Single-Cell Genomics at Fluidigm, said, "Fluidigm is privileged to be partnered with GIS to develop CORTAD-seq, using microfluidics on the C1 system. This novel single-cell, multi-omic technology will help the characterisation of the tumour microenvironment at single-cell resolution and will thus help studies in cancer and immuno-oncology."

Professor Ng Huck Hui, Executive Director at GIS, said, "We are delighted to be working with NCCS and Fluidigm Corporation to develop this novel technology. Such cross-boundary collaborations allow us to further our capabilities and break new frontiers in genomic science. Doing so will also help us better understand how cancer works, and will help bring about better healthcare outcomes for Singaporeans."

IMAGES



Dr Kong Say Li and Dr Li Huipeng, the lead authors that developed CORTAD-seq on Fluidigm C1 microfluidic system, at Single Cell Omics Centre, Genome Institute of Singapore.

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Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Clinical Chemistry*, under the title, “Concurrent Single-Cell RNA and Targeted DNA Sequencing on an Automated Platform for Comeasurement of Genomic and Transcriptomic Signatures” by Say Li Kong^{1,2†*}, Huipeng Li^{3†}, Joyce A. Tai², Elise T. Courtois^{3,4}, Huay Mei Poh^{1,2}, Dawn Pingxi Lau⁵, Yu Xuan Haw², Narayanan Gopalakrishna Iyer⁵, Daniel Shao Weng Tan⁵, Shyam Prabhakar³, Dave Ruff^{6,7}, and Axel M. Hillmer^{2,8*}.

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg.

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As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and research entities, the wider research community and industry. A*STAR's R&D activities span biomedical sciences and physical sciences and engineering, with

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About Fluidigm

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