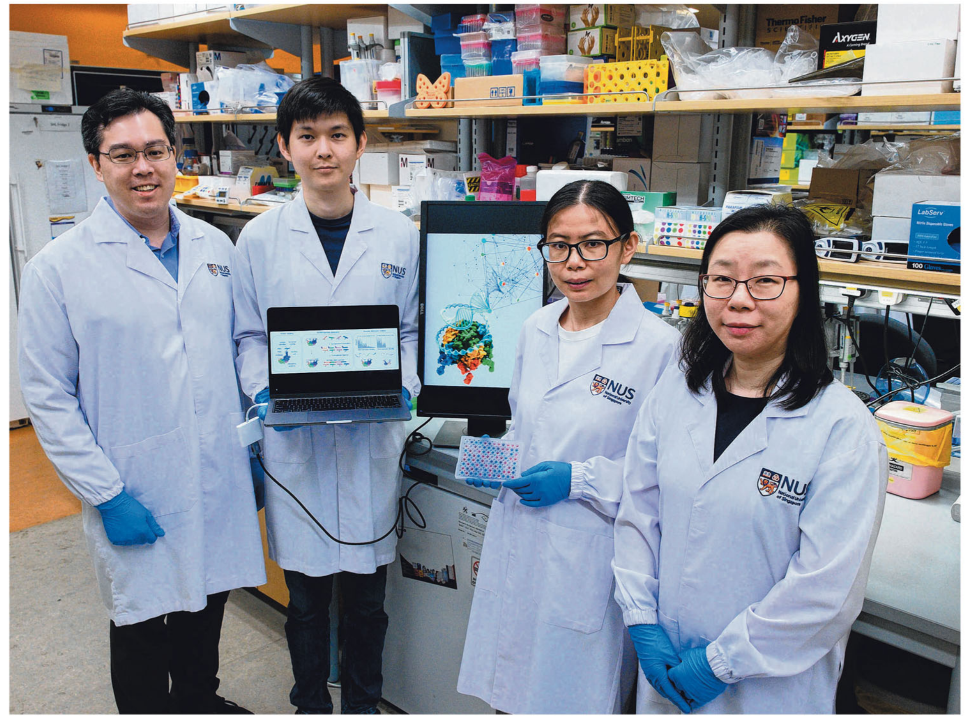
NUS National University of Singapore
Source: *The Straits Times*, pA14
Date: 30 September 2024

New 'Tetris' tech paves way for faster cancer diagnoses



NUS researchers (from left) Brian Lim, Noah Sundah, Liu Yu and Shao Huilin developed Tetris, a novel technology that enables accurate subtyping of cancers, and identifies aggressive forms of the disease, within just a few hours. It has been tested on biopsies of human breast cancer tissues. PHOTO: NUS INSTITUTE FOR HEALTH INNOVATION & TECHNOLOGY

It maps out complex protein interactions that could lead to more targeted therapies

Zhaki Abdullah

The use of DNA helped pieces fall into place for a new technology that could mean faster and more accurate diagnoses of various cancers, as well as more targeted therapies.

Researchers from NUS' Institute for Health Innovation and Technology (iHealthtech) have developed a technology that maps out complex protein interactions within tumour cells.

This allows for greater precision in diagnoses by enabling accurate subtyping of cancers, as well as identifying aggressive forms of the disease, within just a few hours.

Cancer is the leading cause of death in Singapore, responsible for about one in four deaths. More than 84,000 cases were reported here between 2017 and 2021, according to the Singapore Cancer Registry Annual Report 2021.

Believed to be the first of its kind, the technology – dubbed Tandem Elongation of Templated DNA Repeats for Analysis of Interacting Proteins (Tetris) – can lead to more targeted therapies by identifying the specific proteins and interactions that contribute to cancer growth, the researchers said.

Their findings were published in peer-reviewed scientific journal Nature Biomedical Engineering in June.

Noting that protein interactions are responsible for almost all basic life processes, the researchers said understanding such interactions can have wide-ranging clinical applications, from greater accuracy in diagnosing diseases to the development of more effective therapies.

This is in line with the aims of precision medicine, where factors such as genetics, lifestyle and environment are taken into account to provide more targeted treatments.

Current methods for studying protein interactions have limitations, including inaccurate results and incomplete profiling of such interactions.

Yeast-two hybrid assays – considered the current gold standard – test for physical interactions between two proteins or between a protein and a DNA molecule but require genetic manipulation.

They are also limited to studying interactions between two proteins.

Another method, mass spectrometry-based proteomics, tends to miss weak protein interactions.

The researchers noted that both methods fail to capture the full range of protein interactions, particularly higher-order interactions where multiple proteins interact to form large functional assemblies. Changes in such interactions are often linked to more aggressive types of cancer.

The researchers tapped DNA nanotechnology, which refers to the development of artificial nucleic acid structures to be used as novel biomaterial for various purposes.

Associate Professor Shao Huilin from iHealthtech, who led the design of Tetris, said: "DNA is a programmable material and can be used to encode rich information while having predictable interactions, which enables us to craft sophisticated architectures with fine spatial control at the nanometre scale."

The technology, named after the popular video game Tetris, employs what the researchers refer to as Tetris units – molecular nanostructures that comprise antibodies – which target proteins and DNA "barcodes", which serve as identifiers.

Just as players in the game earn points by lining up falling blocks to make them disappear, Tetris units line up according to the patterns of interacting proteins, with the barcodes connecting to their neighbours.

Associate Professor Brian Lim from the NUS School of Computing, who led the development of algorithms used to process data collected by Tetris, said: "This creates a chain of interactions that we can subsequently read and decode via algorithms."

The technology has been tested on biopsies of human breast cancer tissues, from which it accurately diagnosed cancer subtypes and uncovered higher-order protein interactions associated with cancer aggressiveness.

Tetris can also use existing laboratory infrastructure to process large numbers of samples and quickly generate results, allowing it to be integrated into routine clinical workflows with little disruption.

For example, in a doctor's office, the technology can rapidly analyse samples obtained via fine-needle aspiration – a minimally invasive biopsy where a thin needle and a syringe are used to pull out cells, tissue and fluids.

The researchers plan to expand the application of Tetris to other types of cancers and neurological diseases.

They have filed two patents and hope to commercialise the innovation, with Prof Shao expecting it to be more widely available in the next five years.

azhaki@sph.com.sg