

## ScienceTalk Fighting cancer and the 'fog' it brings



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For The Straits Times

A man in his 20s had completed chemotherapy for his early-stage Hodgkin lymphoma, a cancer of part of the immune system.

He wanted to resume his doctoral studies, but found it hard to focus and he was worried that he would have to drop his studies.

A woman in her late 30s used to be able to do calculations quickly at different gambling tables, a skill required of her job as a dealer in a casino.

After she had surgery for early-stage breast cancer, she was prescribed an anti-hormonal drug, and found herself having trouble multitasking. She was hesitant to inform her employer about her condition, as she was worried about losing her job.

An accountant who was in her early 50s complained of constant tiredness and poor memory after going through chemotherapy for breast cancer.

I have worked with these three cancer survivors in my clinical practice at the National Cancer Centre Singapore. All three share similarities. Their cancers were treated at an early stage, and were cured.

They survived their cancer battles, yet, when they tried to resume their normal life, they had cognitive difficulties.

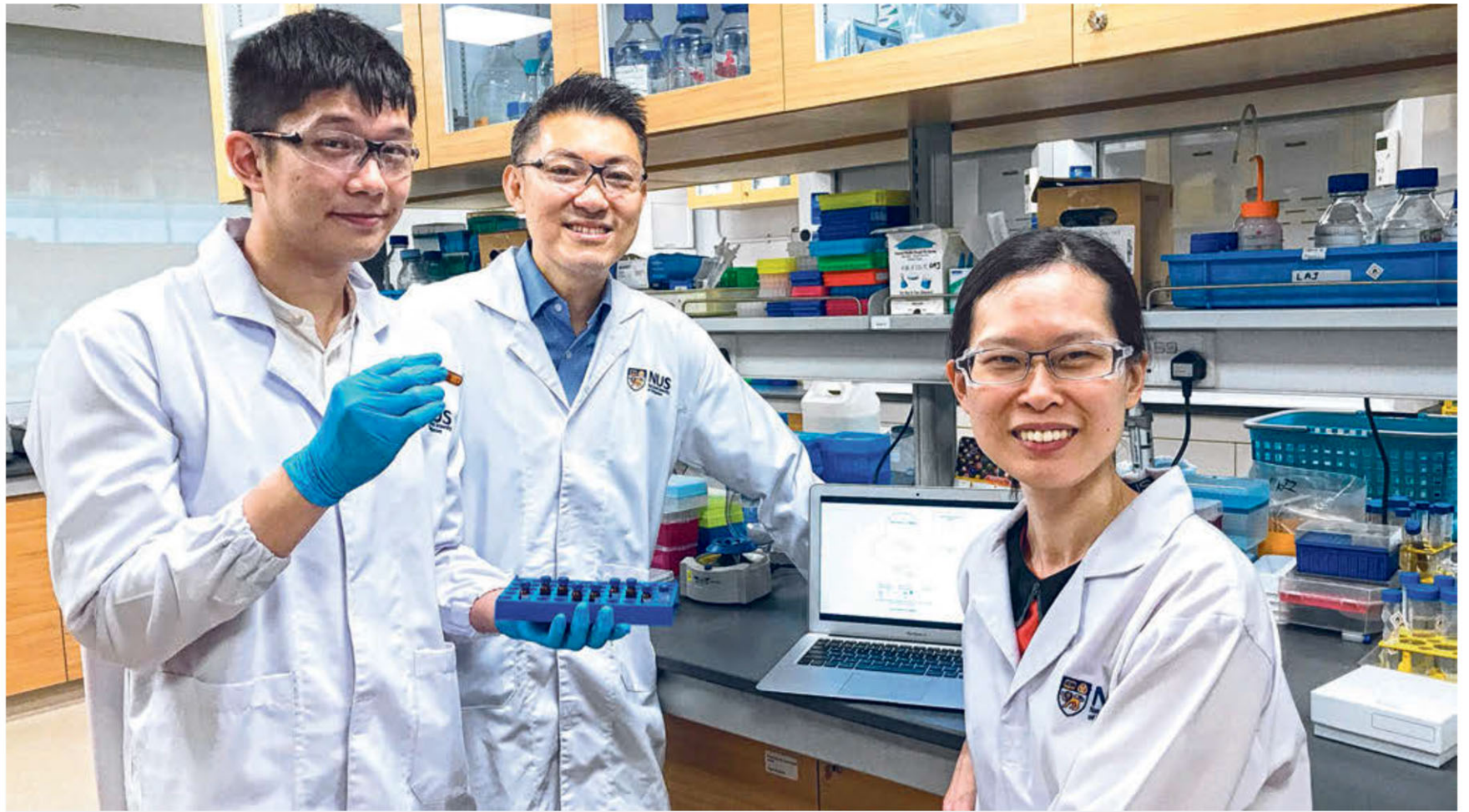
The condition they have is known as cancer-related cognitive impairment (CRCI), more commonly called "chemobrain" or "chemofog".

In the late 1990s, clinicians associated cognitive change with cancer survivors who had undergone chemotherapy only.

However, recent studies in the past decade showed otherwise, with 20 to 30 per cent of patients presenting lower-than-expected cognitive function at the point of cancer diagnosis.

In fact, current research indicates that the prevalence of chemobrain can range from 16 to 75 per cent, depending on how the research is conducted.

The complication of CRCI is significant to individuals, families



(From left) Mr Toh Yi Long, Associate Professor Alexandre Chan and Assistant Professor Lau Aik Jiang are part of a team that is studying the effects of hormone levels on chemobrain among adolescents and young adult cancer patients. PHOTO: NATIONAL UNIVERSITY OF SINGAPORE

### Effects of hormone levels on chemobrain

Anti-hormonal therapies are used to slow down tumour growth and stop cancer cells from multiplying, in certain cancers such as breast cancer.

There are concerns, however, that suppressing hormone levels over time may affect the cognitive function in cancer patients and survivors, due to the role of hormones

in healthy mental processing.

In a study conducted by Mr Toh Yi Long, a doctoral student at the NUS Department of Pharmacy, breast cancer patients with higher levels of dehydroepiandrosterone and its sulfated form, jointly known as DHEA(S), were reported to be at lower risk of developing self-perceived cognitive impairment.

DHEA(S) are the main precursors related to the biosynthesis of testosterone and oestrogen.

Mr Toh and his colleagues plan

to study the effects of hormone levels on chemobrain among adolescents and young adult cancer patients. Such a study is crucial as these patients are in their developmental stages, and cognitive complications may cause them significant lifetime impact.

### GENETICS OF CHEMOBRAIN

Genetic polymorphisms are slight variations in a person's genetic make-up, and some of them can influence the susceptibility of de-

veloping cancer-related cognitive impairment.

The research group has identified one such polymorphism in the brain-derived neurotrophic factor (BDNF) gene. The BDNF gene is involved in the production of its protein BDNF, which regulates the function and development of brain neurons.

Mr Tan Chia Jie, a doctoral student at NUS' Department of Pharmacy, examined a group of cancer patients who have a variation of

this gene, called Val66Met, and found that they report less cancer-related cognitive impairment after undergoing chemotherapy.

Similar results were found in two different cohorts of breast cancer patients in Singapore.

The findings can help clinicians identify patients who are likely to experience cancer-related cognitive impairment, so that there can be intervention to maintain their cognitive abilities during and after chemotherapy.

and society. In the United States, up to 53 per cent of cancer survivors between 16 and 39 years old face problems such as memory and attention deficit at school and at work.

Such impairment contributes to serious issues in the workplace.

To examine the impact of chemobrain on Asian populations and what can be done for our cancer survivors, over the last decade, my research team at the Department of Pharmacy at the National University of Singapore (NUS) has conducted numerous studies involving several local cancer populations.

In two cohorts of more than 400 breast cancer patients, we observed differences in cognitive decline among individuals over a one-year period after chemotherapy treatment ended.

One out of six patients reported cognitive decline during chemotherapy, yet cognitive function recovered soon after the end of

chemotherapy.

About one in four patients experienced either cognitive impairment at the end of treatment that persisted up to one year after treatment, or cognitive impairment that surfaced only much later after the end of treatment.

Symptoms can appear quite early in some patients, but not all patients were equally affected by the same type of chemotherapy treatment.

Our analyses have also shown that patients who report cognitive changes are more likely to also experience anxiety and fatigue.

Knowing their symptoms is important to clinicians because intervention to correct a co-existing symptom can potentially affect the severity of chemobrain.

We have looked at the data we collected from the participants' blood samples, to ascertain if there are any signalling pathways (a group of molecules in a cell that work together to control one or

more cell functions) are associated with chemobrain.

Understanding the pathways underlying chemobrain can help us develop therapeutic approaches.

In two studies, we found that pro-inflammatory cytokines – signalling molecules that promote inflammation – are associated with cognitive changes. This may explain why aerobic exercise, which has anti-inflammatory effects, may reduce the risk of CRCI.

In another study, we found that patients who are more prone to cognitive impairment have a more drastic reduction of brain-derived neurotrophic factor (BDNF) in their blood. This is a protein that controls the growth and function of nerve cells in the brain and spinal cord.

Aerobic exercise can also induce BDNF levels. My team at NUS is currently conducting studies to evaluate whether routine exercise during chemotherapy could raise BDNF levels among our cancer

patients.

Concurrently, we are examining the brain images of both patients and healthy individuals, to understand how cancer and chemotherapy impact the various parts of the brain, which in turn affects cognitive function, and how the various signalling pathways affect the brain structures.

We are developing and testing interventions to help cancer survivors who are suffering from cognitive changes.

This involves identifying the group of patients who would benefit from early rehabilitation, as well as identifying the most optimal mode and timing of cognitive rehabilitation.

Cancer survival is a lifelong journey with a huge emphasis on improving wellness so that normal life can resume. Survivorship care plans that address patients' well-being after cancer treatment are important.

The current lack of effective

pharmacological treatment options available to manage this problem means there is an urgent need to translate our results back to clinical practice. Since cognitive needs can differ greatly among cancer survivors, back-to-work programmes and training must be personalised and tailored to each survivor's needs.

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