

Unlocking the secrets of gastric cancer

S'pore team pinpoints the stem cells behind the disease that's called a silent killer



Chang Ai-Lien
Senior Correspondent

Four years ago, Ms Constance Tan felt hale and healthy, with absolutely no symptoms of being ill. But when she went for an endoscopy as part of a routine check-up, the thin, flexible tube peering into her stomach showed that all was not well. Then came the shocking news.

Doctors found that she had early-stage stomach cancer, and to save her life, they cut out her entire stomach.

"Everything is fine now, it took only six months to get my life back to normal," said Ms Tan, a consultant in her 50s.

She is very lucky.

Stomach cancer, also known as gastric cancer, is called a silent killer as it is usually discovered only at an advanced stage. About 500 people here are diagnosed with it every year, and half suffer a relapse even after treatment.

"Even if you're feeling great you should still go for your yearly check-ups," stressed Ms Tan, who said she was happy to donate her gastric tissue to researchers searching for better ways to diagnose and treat the disease.

Thanks to patients like her, a team from Cancer Science Institute of Singapore (CSI-Singapore) at the National University of Singapore, and the National University Hospital has amassed one of the world's largest collections of gastric cancer tissue.

And after five long years, the team has found a biomedical needle in a haystack.

Sifting through billions of cells, the scientists have discovered, for the first time, the stem cells that cause stomach cancer.

Cancer cells are not homogeneous, and many researchers believe that within a tumour, a few act as stem cells that reproduce them-



(From left) Dr Chan Shing Leng, research assistant professor at the Cancer Science Institute of Singapore at NUS; Ms Constance Tan, a former gastric cancer patient who donated her tissue for research; and Associate Professor Jimmy So, a senior consultant at NUH's Department of Surgery. Ms Tan's cancer was discovered at an early stage. The disease is more often discovered only at an advanced stage. About 500 people here are diagnosed with it every year.

ST PHOTO: KEVIN LAM

selves and sustain the cancer, much like how normal stem cells renew and sustain organs and tissues.

But out of the hundreds of thousands of cancerous cells in a typical patient, only a tiny fraction are cancer stem cells capable of regenerating. So the sprinkling of cancer stem cells hiding within the mass of tissue can be missed by conventional treatments, which is why the cancer returns.

The Singapore researchers started out with a clue—looking at a protein on the surface of cells called CD44, because it has been fingered in many cancers. But, explained NUH senior consultant Jimmy So, this protein is too widespread as it is also found in other normal cells such as white blood cells.

"If we target all cells with CD44 the side effects would be terrible," said Associate Professor So, who is

GASTRIC CANCER SYMPOSIUM

Stomach cancer is the second leading cause of cancer death worldwide, and is particularly common in Asia. But it does not get as much attention as other cancers more prevalent in the West.

In Singapore, gastric cancer ranks among the top 10 cancers, with about 500 new cases a year. Three in four patients have their disease discovered at a late stage, by which time it becomes very difficult to treat.

As part of Gastric Cancer Awareness month, the Singapore

Cancer Society and National University Cancer Institute Singapore (NCIS) are organising a Gastric Cancer Awareness Public Forum.

It is free, and will be held at the Lee Kong Chian Auditorium in YMCA International House on Aug 30, with an English session from 1pm to 2.30pm, and one in Mandarin from 3pm to 4.30pm.

In addition to talks by doctors and dietitians, it will feature videos on healthy cooking.

Those who would like to attend can call 6421-5804 or send an e-mail to education@singaporecancersociety.org.sg, with their name, contact number, e-mail address and language of the forum they would like to attend, to register.

Doctors can also attend the free Gastric Cancer Awareness Month GP Forum 2014 this Saturday.

It is being held at Swissotel Merchant Court Hotel from 1pm to 4pm.

Chang Ai-Lien

with the hospital's surgery department, and a key member of the research team.

To get the cells they needed, the

researchers collected the tissue after an operation, rushed back to the laboratory, processed it and grew cell colonies in special mice with

no immunity. Then they separated the various cells by suspending them in a stream of fluid and passing them by an electronic detec-

Go for yearly checks
"Everything is fine now, it took only six months to get my life back to normal... Even if you're feeling great you should still go for your yearly check-ups."

MS CONSTANCE TAN, who had early-stage stomach cancer

tion apparatus.

These different cells were then injected into mice to see if tumours formed.

Through this tedious process the group managed to tease out a CD44 variant—called CD44v8-10—which occurred only in gastric cancer cells, not normal tissue.

"It is very aggressive. If you introduce it into cells, as few as 20 cells can cause a tumour," said Prof So, who is also head of the Upper GI Tumour Group at the National University Cancer Institute, Singapore.

Next in line, said lead researcher Chan Shing Leng, is a drug that will zoom in on that specific protein variant, which she believes will be a powerful weapon against cancer that can be used in combination with chemotherapy.

"We already have an antibody now that can recognise such cells, but it cannot kill them," said Dr Chan, a CSI-Singapore research assistant professor.

"So more engineering is required, and we're working with researchers at the Agency for Science, Technology and Research to fine-tune compounds and biologics that can be used in detection and therapy."

Biologics are medicines made from organic material.

Even more exciting, CD44v8-10 could also hold the key to tackling colon, breast, pancreatic and other cancers.

"I believe our work opens a critical window for targeting cancer stem cells in other cancers," she said.

Added Prof So: "I believe we will see this work making a difference in patients before my career ends."

The team's breakthrough was published in the journal *Cancer Research*. And cancer survivor Ms Tan is delighted with the news, and her role in it.

"It feels fantastic," she said. "I'm grateful to them for being involved in this kind of meaningful work, something which gives people reassurance that cancer can be manageable and curable."

allen@sph.com.sg

Beautiful Science

A tumour sphere grown from a piece of tissue donated by a National University Hospital stomach cancer patient reveals some of its secrets. A particular protein found in gastric cancer cell membranes shows up here as green, while the cells' DNA is stained blue. This patient has a mutation in the tumour suppressor gene p53, resulting in abnormally high levels of malfunctioning p53 protein (red), which cannot do its job of keeping the cancer in check. These tumour cells grown in the laboratory allow researchers to study what makes stomach cancer so difficult to treat, and to develop drugs to fight it.

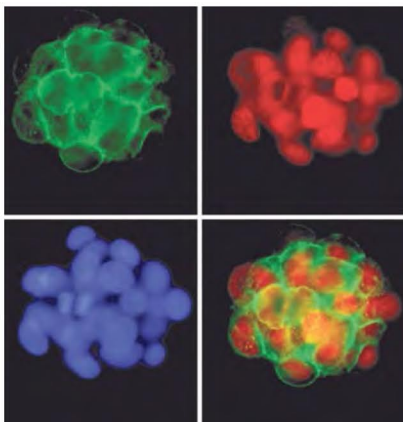


PHOTO: CHAN SHING LENG, CSI-SINGAPORE, NUS