GAINING GROUND IN THE WAR ON CANCER

EARLY DIAGNOSIS OF PANCREATIC CANCER and A NEW WAY OF TREATING HARD-TO-REACH LUNG TUMOURS are two ways that researchers in Japan are advancing on problematic cancers.

Nearly one in six deaths globally each year is the result of cancer. While much progress has been made in preventing, screening, diagnosing and treating this complex, varied and challenging disease, there is still far to go.

In accordance with its founding principle of *Saisei-Kyumin* ("to save people everywhere"), the Nippon Medical School is dedicating much of its research expertise to study cancer prevention and treatment.

As Japan's oldest private medical school, established in 1896, the Tokyo-based institute has long distinguished itself as a research facility that brings the very latest technologies to bear on medical research challenges.

Nippon Medical School has tried to develop novel medicines with both sides of basic and clinical medical sciences.

CATCHING A KILLER EARLY

One example is the work being done by Kazufumi Honda, a professor in cancer research, to identify biological signatures of early-stage pancreatic cancer. Pancreatic cancer is one of the most deadly cancers, as by the time it is diagnosed, the disease is typically well advanced. Its symptoms include weight loss, loss of appetite, abdominal pain and changes in bowel habits. But since these symptoms are both vague and common in the general population, pancreatic cancer is hard to uncover.

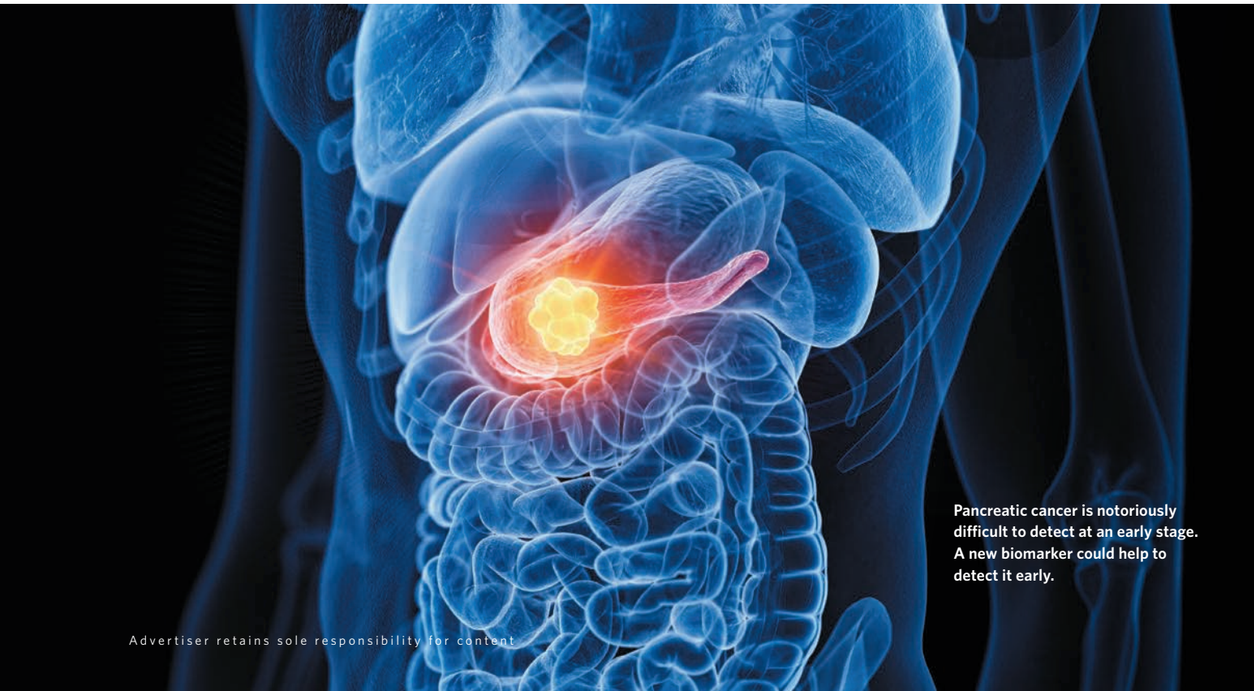
If it is diagnosed at stage I, before the cancer has spread beyond the pancreas, patients have a five-year survival rate of nearly 50%. But if it's diagnosed at stage IV, the five-year survival rate slumps to 1%.

Honda and his colleagues have used an approach called proteomics — the study of the behaviour of proteins in the body — to help develop a non-invasive diagnostic test for early-stage pancreatic cancer. Using an analytic technique called mass spectrometry, which enables a detailed analysis of all the molecules in a sample, they identified key differences in the levels and activity of proteins between patients with pancreatic cancer and healthy controls.

In particular, they looked at a type of protein called apolipoprotein A2, and found that cancer patients process this protein differently to controls. These differences were also seen in people who didn't have pancreatic cancer, but were at high risk of the disease because they have a condition known as intraductal papillary mucinous neoplasms.

This suggests that analysing levels of this biomarker could be used to screen people for early-stage pancreatic cancer and identify those at high risk of developing it. These people could then be examined more closely using imaging technology, which is accurate but expensive.

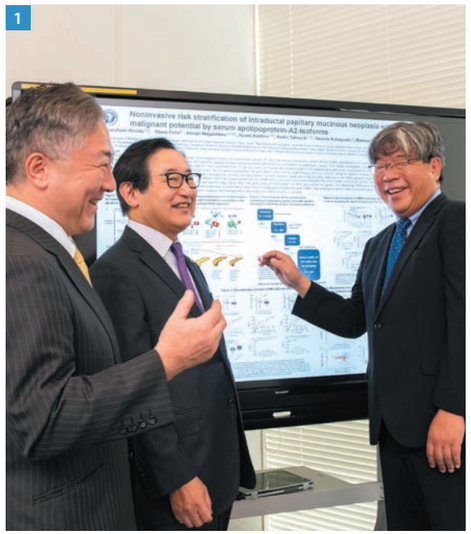
"To efficiently establish pancreatic cancer screening in the general population, we have to identify pancreatic cancer high-risk people from the general population by using this minimally-invasive biomarker," Honda says. Having been approved by the Japanese government for *in vitro* diagnostics, the test will soon be available for clinical use.



Sebastian Kaulitzki/Science Photo Library/Getty

Pancreatic cancer is notoriously difficult to detect at an early stage. A new biomarker could help to detect it early.

ADVERTISEMENT FEATURE



Jasmin Merdan/Moment/Getty

▲ **1. Jitsuo Usuda (left), Akihiko Gemma (centre), and Kazufumi Honda (right).**
2. Minimally invasive blood tests for a biomarker for pancreatic cancer could help to detect the cancer earlier.
3. Plasma samples for biomarker development.

HARD-TO-REACH TUMOURS

Early detection is one of the pillars of cancer research. Treatment is another. In the case of lung cancer, there are numerous forms of chemotherapy, but patients often have to undergo surgery to remove the tumour, which can include removal of a section of lung. This can have long-term effects on lung function, and can be particularly risky for older patients, those with pre-existing lung disease, or those with heart disease.

A less invasive option is photodynamic therapy, in which the tumour is infused with a light-sensitive medication, then treated with lower-powered laser therapy that activates the medication and destroys the tumour. This works well for tumours in the central part of the lung because this region is relatively easy to reach with the laser using a bronchoscope that is fed down the main airways. But so far it hasn't been possible to use this approach for smaller tumours that are deeper in the lung, because they can't be reached using a traditional bronchoscope.

Now, bioengineer Jitsuo Usuda and his colleagues have developed a way to reach these small peripheral tumours using a new type of flexible laser probe. Not only is the probe able to reach deeper into the lung, but the laser frequency used is better at penetrating to the heart of the tumours.

The first clinical trial of this approach in 7 patients with peripheral lung cancer has shown promising results. An investigator-initiated clinical trial of photodynamic therapy for peripheral type lung cancer was conducted on 54 patients to apply for approval. This study was conducted on patients who were refractory to surgery or radiotherapy, and it is currently under follow up for the primary endpoint of progression-free survival.

Usuda says the treatment could mean some patients with small, early-stage cancers might be able to avoid surgery altogether. "The important thing is to maintain the quality of life and preserve the lung function, so non-invasive treatment is needed for lung-cancer patients," he says.

To understand the effect of treatments, researchers look not just at what happens to the patient's body but also the biochemical changes taking place inside the tumour and what those changes mean in terms of treatment outcomes.

"THE IMPORTANT THING IS TO MAINTAIN THE QUALITY OF LIFE AND PRESERVE THE LUNG FUNCTION."

A VALUABLE RESOURCE

This is where Nippon Medical School's rebiopsy bank becomes vital. Set up by the school's president and oncologist, Akihiko Gemma, this tissue bank stores consecutive samples taken from tumours before, during and after treatment. The hope is that by collecting these tissue samples using special systems with accurate and detailed clinical data, researchers can use them to understand how tumours change in response to treatment, how they might develop resistance to treatment, and how that resistance might be overcome with other treatment approaches.

Established in 2013, the rebiopsy bank now has more than 9,600 tissue and blood samples from Japanese patients with colorectal, lung and blood cancers. These samples have been used by a network of basic and clinical researchers to explore issues such how circulating cell-free DNA can be detected in the blood of patients with colorectal cancer, or what role non-coding RNA plays in the resistance, spread and recurrence of lung cancer.

"Our aim is to shed new light on cancer treatment," says Gemma. "And we're seeking to do this by developing therapies such as immunotherapy that lead to the prevention and control of treatment resistance." ■

日本医科大学 NIPPON MEDICAL SCHOOL

www.nms.ac.jp/college/english