A new model for pancreatic cancer research

In a lab at UNSW, a TCRN-supported project is on the precipice of revolutionising pancreatic cancer research.

The project, a novel pancreatic cancer model, is based on patient-derived, surgically resected pancreatic tumour tissue from patients undergoing surgery at Prince of Wales and Prince of Wales private hospitals.

What sets it apart from similar models is that it recreates not only the tumour itself but the surrounding tumour environment, which plays a critical role in enabling cancer metastasis and hampering the delivery of therapeutics to the tumour site.

"We know that pancreatic cancer is so deadly, not necessarily because of the tumour cells only but because of the surrounding fortress – that's really a key player in driving the aggressive nature of the disease," says project participant and UNSW Scientia PhD John Kokkinos, who was also the primary first author on a recent article about the work published in *Scientific Reports*.

"So, we wanted to find a way to model that whole environment in the lab rather than breaking it apart and studying individual cell types by themselves."

Personalising cancer care

The work is focused on pancreatic ductal adenocarcinoma, a malignancy that makes up about 85 per cent of all pancreatic cancer diagnoses in Australia. However, the team has also successfully grown models of rare pancreatic cancer subtypes using the same innovative model.

In partnership with his supervisor, internationally acclaimed pancreatic cancer researcher Associate Professor Phoebe Phillips, Kokkinos is using the model to study the biology of the tumour, as well as its response to different types of drugs. The process provides an extraordinary opportunity to investigate the use of more personalised treatments that respond to each tumour's unique characteristics.

"We can test different chemotherapy drugs, we can test the new drugs that we're developing in the lab, we're collaborating with other industry partners now to test other clinical-grade therapeutics," Kokkinos says.

"It can give us a bit more confidence in translating these pre-clinical drugs to the clinic, and also it can potentially help us predict which drugs will be effective on each individual patient."

Bringing clinicians and academics together

The research is the result of an innovative collaboration between Kokkinos and Phillips; hepatopancreatobiliary and transplant surgeon Dr Koroush Haghighi, also a member of the TCRN; and TCRN staff involved with the day-to-day administration of the HSA Biobank, who coordinate the consent and tissue transfer processes. To date, Phillips's team have received more than 70 tissue samples for use in the model.

When a patient is booked in for pancreatic cancer surgery with Dr Haghighi, they are asked to consent for some of their tumour tissue to be given to the HSA Biobank. The surgical team notifies the biobank team, who arrange for the tissue to be brought back to the lab within 15 minutes of resection.

Once the tumour sample arrives at the lab, the work can begin: using a scalpel, Kokkinos cuts the tissue into 1–2-millimetre pieces and places it on a scaffold through which the tissue can continue receiving nutrients to keep it alive.

Incredibly, these tumour slices, called 'explants', can maintain their original structure and characteristics for 12 days in the laboratory environment. By contrast, a similar model that used thinner tissue slices was only viable for 96 hours, with the samples beginning to degrade as early as 24 hours.

"We think our model better maintains the structure and viability and proliferation of all the cell types," Kokkinos says.

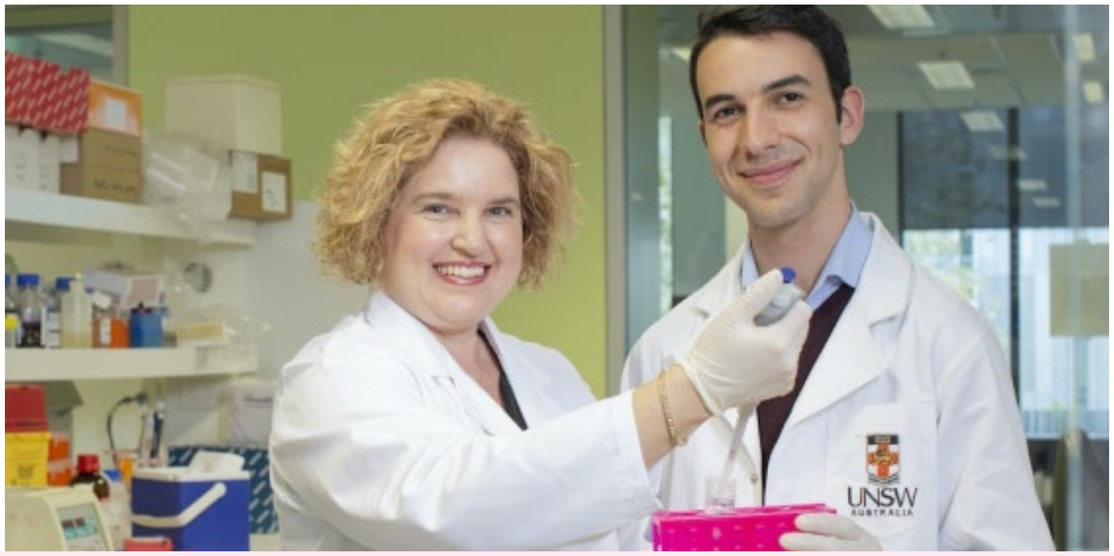
Infrastructure that supports innovation

Pancreatic cancer remains a challenging proposition for researchers. Despite its increasing prevalence – rates in Australia have more than doubled over the last 20 years, according to the AIHW, and the disease itself has a five-year survival rate of less than 10 per cent – it remains persistently difficult to treat.

Novel approaches like this one have the potential to significantly shift the way pancreatic cancer is diagnosed and treated.

The project is just one example of the expanding remit of the HSA Biobank, which was originally established as to store tissue collections and linked patient data for use by translational cancer researchers.

In response to the changing research landscape, the TCRN is currently leading the development of new research initiatives designed to expand the biobank's remit. These include pilot projects to explore the feasibility of bioimage banking and the collection of stool and oral swab specimens for microbiome research, among others.



Associate Professor Phoebe Phillips and UNSW Scientia PhD John Kokkinos. Image credit UNSW

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John Kokkinos