Melbourne surgeon to conduct world leading immunotherapy trials



Victorian Colorectal Surgical Trainee and PhD candidate Dr Joseph Kong has received industry funding to conduct one of the first trials in the world of an immunotherapy agent - currently being tested in advanced lung and pancreatic cancer - to treat patients with locally advanced rectal cancer (LARC).

The recipient of a number of RACS scholarships, Dr Kong has spent the past three years conducting PhD research aimed at finding immune markers to predict response in patients with LARC to neoadjuvant therapy and the use of immunotherapy in treating the disease.

His work has proven promising and in the last few months Dr Kong, with collaborators including medical oncologists, radiation oncologists and surgeons, has successfully submitted and obtained a grant to conduct Phase 1/2 clinical trials on PD-L1 blockade in combination with chemoradiotherapy at the Peter MacCallum Cancer Centre (PMCC) in Melbourne.

Dr Kong said he was delighted with the news of the grant but that much work was still needed to set up the clinical trial, which would require months of preliminary ethics and design work before commencement. He said the first trial would likely include ten patients while the Phase 2 study would incorporate more patients and other cancer centres around Australia.

"This will be one of the first trials in Australia where an immunotherapy agent is tested in patients with LARC which is very exciting," he said.

"Patients who will gain the most benefit will be those who did not respond to neoadjuvant chemoradiotherapy which represents around 20-30 per cent of all LARC patients. We hope this work will improve their overall and disease-free survival as these patients have exhausted all conventional clinical treatments with no other alternatives available to improve tumour response rates. "We are now in the process of designing the trial to determine the best way of incorporating immunotherapy in the neoadjuvant setting in terms of timing, frequency of delivery and dosage."

Dr Kong said he had undertaken his PhD research because while Australia has the highest rates of bowel cancer in the world with the disease being the second most common cause of cancer death, there were few methods to determine which patients would get the most benefit from neoadjuvant therapy.

He said that while up to 30 per cent of patients with LARC showed a complete response to current clinical treatments – including resection and chemoradiotherapy – a significant number of patients showed poor to little response with correspondingly poor overall survival.

As such he set out to:

- Validate known methods in quantifying immune cells in LARC and to correlate that with response to neoadjuvant chemoradiotherapy;
- Develop a novel functional immune assay using rectal cancer organoids and matched tumour-derived tumour infiltrating lymphocytes to predict response to treatment; and
- Develop methods to incorporate immunotherapy in the neoadjuvant setting for LARC as an alternative method to increase the tumour response rate.

As clinicians, we strive to improve patient outcomes and minimise harm from therapies that have significant side effects. Being able to stratify patients into specific treatment pathways is at the forefront of medical care.

Now in the process of writing up his thesis, Dr Kong said that while some cancer centres around the world were offering patients with LARC neoadjuvant treatment only without surgery, up to ten per cent of the patients who were deemed in complete remission have tumour regrowth.

CAREER HIGHLIGHTS: GRANTS, AWARDS & SCHOLARSHIPS

2017:

Clinical Trials Phase I/II of PD-L1 blockade 2017: RACS Paul MacKay Bolton Scholarship for Cancer Research

2016:

- RACS Foundation for Surgery John Leowenthal Research Scholarship
- Young Investigators Award Surgical Research Society for best research paper

2016:

CSSANZ Foundation Grant to investigate methods or predict response in LARC

2016 – 2018: NHMRC Post Graduate Scholarship

2015: RACS Raelene Boyle Research Scholarship

He said current diagnostic modalities to confirm complete tumour regression relied on conventional tests – such as colonoscopy, biopsy and/or imaging – which were limited in their ability to predict response accurately.

Woking at the Division of Cancer Research at the PMCC and the University of Melbourne, Dr Kong uses fresh tissue samples obtained by biopsy to grow tumours in the laboratory which he then tests with a range of molecular compounds including immunotherapy to see which had the greatest impact on tumour cells.

"This is personalised medicine, which is designed to provide patients with the best possible treatment regime," Dr Kong said.

"As clinicians, we strive to improve patient outcomes and minimise harm from therapies that have significant side effects. Being able to stratify patients into specific treatment pathways is the forefront of medical care.

"As an example, patients with complete response to neoadjuvant therapy may avoid surgery completely, eliminating the risk associated with surgery.

"However, this 'watch and wait' approach is not routine clinical practice and there is still a pressing need to identify an accurate predictive tool."

Dr Kong received his FRACS in 2014 and is now in the Colorectal Surgical Society of Australia and New Zealand (CSSANZ) training stream.

He has conducted his research under the supervision of Professor Alexander Heriot, Director of Cancer Surgery at the PMCC, Professor Robert Ramsey, Head of the Differentiation and Transcription Laboratory at PMCC, and Professor Wayne Phillips, Head of PMCC's Cancer Biology and Surgical Oncology Research Laboratory.

SUCCESSFUL SCHOLAR

Dr Kong completed his medical training in New Zealand and his surgical training in Australia. He has a Master of Surgery Degree and has received a number of awards, scholarships and grants in recent years.

Last year he was awarded the RACS Foundation for Surgery John Loewenthal Research Scholarship, which is awarded to Fellows undertaking research in any cancerrelated field and won the prestigious Young Investigator Award at the Surgical Research Society held in Melbourne. The award provides Dr Kong with the funds to attend the Association for Academic Surgery/Society of University Surgeons Congress and to present his work in the United States in 2018. Dr Kong thanked the College and Fellows for their support.

"While I have missed surgery, I believe that this research has the potential to help patients by refining diagnostic tools and developing novel therapies, which can hopefully improve patient outcomes," he said.

"It's extremely stimulating to confront complex problems and answer clinical research questions through translational research, which plays a small part in a global effort to advance our understanding of, and treatments for, cancer.

"The support I have received from the RACS has been invaluable and greatly appreciated because it allowed me to fully concentrate on my research which has, in turn, led to the clinical trials that we expect to run next year."

- With Karen Murphy



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Opportunity to join a long established (34 years) practice of a sole surgeon practitioner and subsequently take it over. The principal plans to retire by the end of 2017. Training will be provided in the transition period. This position would suit an orthopaedic or general surgeon, especially one looking for reduced working hours and a great lifestyle.

Contact Zahria on 0402026290