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IMPROVING THE ODDS

Dr Matthew Read has used his scholarship to develop the knowledge on an extremely aggressive cancer



Surgical Trainee Dr Matthew Read has designed a novel in-vivo model for researching oesophageal adenocarcinoma (OAC) and its precursor condition, Barrett's oesophagus (BO).

Using his surgical skills, Dr Read solved a problem facing many researchers in the field of OAC by designing a technique that allows patient-derived tumours to grow and develop in intra-muscular pockets of immunocompromised mice.

By implanting tumours in a more vascular environment than the previous subcutaneous location, Dr Read has dramatically improved the success rates of patient-derived OAC tumour xenografts from 35 per cent up to an efficiency rate of nearly 95 per cent.

He said that while OAC was an extremely aggressive cancer with a poor

prognosis, the design and development of new therapies was being hampered by the difficulty in studying the disease and the consequent lack of knowledge relating to the biology of the cancer.

“One of the most powerful research models currently being used in other cancer streams is the patient derived tumour xenograft (PDTX) which have been well characterised and shown to be representative of the original patient tumour,” he said.

“However, there has been only minimal success in generating PDTX from OAC with only five studies reporting the successful generation of PDTX in OAC with a success rate ranging between 30 to 35 per cent.

“Through the development of this novel technique of tumour tissue

placement, we have managed to improve the efficiency of tumour transfer to nearly 95 per cent. This is because the improved blood supply within the intramuscular environment supports the tumour until it can develop its own blood supply. Validation has since confirmed that this model is representative of the original tumour with respect to tissue architecture, molecular and genetic profile and tumour biology.”

Dr Read, a SET4 Trainee, said there was a growing urgency to advance research into OAC because it had the fastest rising incidence rate of any solid cancer over the past four decades. As a result, there were six laboratories in Australia alone now collaborating on OAC. That urgency also extended to enhancing understanding of BO, a precursor condition in which the normal stratified squamous lining of the lower oesophagus is replaced by columnar epithelium.

He said that while BO occurred in five per cent of the population, it conferred between a 30 to 100-fold increased risk in the development of OAC, which has a current five-year survival rate of only 16 per cent.

Dr Read said one of the great advantages of the new in-vivo model was that it would allow for the rapid growth of multiple patient-derived tumours upon which to test new drug therapies, a process that would otherwise have taken years given the previous low successful tumour transfer rates.

Dr Read said he was using the new in-vivo model to investigate both ends of the disease spectrum in Barrett's carcinogenesis.

“I am using this model to determine the frequency of tumour initiating cells within OAC,” he said.

“These cells have important implications for disease recurrence as they maintain the ability to form new tumours.

“I am also in the process of conducting a series of experiments in an attempt to identify a potential stem cell responsible for the formation of Barrett's oesophagus in the hope that it may lead to advances in the treatment of the condition before it becomes OAC.”

Saw impact of cancer

Dr Read is conducting his research as part of a PhD and received support from the College in 2013 through the Francis and Phyllis Thornel-Shore Memorial Scholarship. He is now receiving funding via the Sir Thomas Naghten Fitzgerald Scholarship offered through the Faculty of Medicine at the University of Melbourne.

Dr Read said that he decided to become involved in research while training under his current research supervisor, Mr Cuong Duong at the Western Hospital.

“As a surgical Trainee I witnessed first hand the terrible impact that cancer has on patients and their families.

“That experience spurred me to accept that only new treatments will improve patient outcomes and that those future treatments depended on current research.”

Dr Read is conducting his research work through the Surgical Oncology Laboratory at the Peter MacCallum Cancer Centre under the leadership of Professor Wayne Phillips and research scientist Dr Nicholas Clemons.

He said that such was the interest, a number of Upper GI Fellows supported his work by allowing him to take tumour tissue at the same time as they conducted patient biopsies or operated to remove OAC tumours.

“Associate Professor Val Usatoff, Mr Paul Burton and Mr Marty Smith at Cabrini, Mr Hai Bui at the Western Hospital and Mr Cuong Duong, Mr John Spillane and Mr Stephen Barnett at the Peter MacCallum have all been extremely helpful and I offer them my thanks,” Dr Read said.

“Professor David Watson in Adelaide has also been a great contributor to this

research as we attempt to establish PDTX from cryopreserved tumour samples.”

Through these collaborations, Dr Read has now grown and studied more than 30 patient-derived tumours using his new in-vivo model.

He is now in the process of writing up papers on his OAC in-vivo research and his BO results, which are unique given that he has successfully xenografted pre-tumour tissue.

He has presented his findings at the ASC in Singapore this year, last year at the ASC in Auckland and at the 13th World Congress of the International Society for Diseases of the Oesophagus held in Venice in 2012.

A father of three, Dr Read said that while it was hard to take the plunge into full-time research, the support he received made the move not only viable but also exciting.

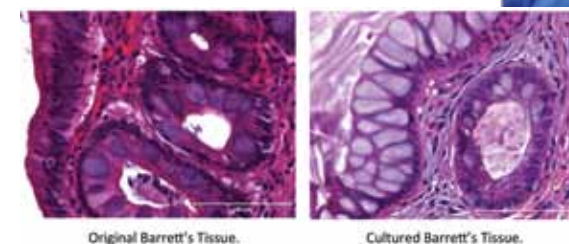
“It's a massive gamble to take research on during training, because you have to make the commitment before you have any guarantee of funding, so I felt very fortunate to receive the scholarships,” he said.

“It's great that the College funds such research at an early stage because in some ways that support is worth more than its dollar value because it represents professional support for your endeavours.

“I have found this research both fascinating and rewarding and it is very exciting to solve a problem and develop a tool or technique that could have a number of applications in a number of research streams.”

The Francis and Phyllis Thornel-Shore Memorial Scholarship was established to promote medical research, has an annual value of \$60,000 and is open to both Fellows and Trainees of the College.

With Karen Murphy



SCHOLARSHIPS

2012 & 2014

Sir Thomas Naghten Fitzgerald Scholarship, Faculty of Medicine, The University of Melbourne

2013

Francis and Phyllis Thornell - Shore Memorial Scholarship - Royal Australasian College of Surgeons

AWARDS

2014

Best Trainee Presentation, Upper GI Surgery Section, Annual Scientific Congress, Singapore.

2013

Prof Robert Thomas Translational Research Award, The Peter MacCallum Cancer Centre.

2013

Best Trainee Presentation, Surgical Oncology Section, Annual Scientific Congress, Auckland.

