THANK YOU

Priority Research Centre for Cancer Research, Innovation and Translation
2018 Career Advancement Fellowships in Cancer Research
Final Report
Thank you for your generous donation to support the career advancement of the early and mid-career researchers of the Priority Research Centre for Cancer Research Innovation and Translation, and Hunter Cancer Research Alliance.

With this support, the four recipients of the 2018 Career Advancement Fellowship have flourished in their postgraduate careers in diverse cancer research fields with enhanced security and confidence. As a consequence, two recipients have this year been awarded competitive external fellowships, one has been funded thanks to a generous pharmaceutical grant and one is continuing in a previously awarded fellowship. This success will allow further research outputs leading to sustainable careers as scientists in the University of Newcastle.

We look forward to a bright future for these Fellows, which has been substantially enhanced by this very welcome benefaction.

Professor Stephen Ackland
Hunter Cancer Research Alliance Director

Thank you for your generous donation to support the career advancement of the early and mid-career researchers of the Priority Research Centre for Cancer Research Innovation and Translation, and Hunter Cancer Research Alliance.
Resistance to therapies remains a significant barrier to breast cancer survival. A breast cancer that is resistant to treatment is impossible to cure. Therefore, there is an urgent need to develop better predictive tests, so that the right treatment is chosen. I am working on a protein called p53. This protein is a well-known cancer suppressor and proper p53 function is essential for the response to DNA-damaging therapies. However, p53 does not work in most cancers. Despite this, DNA-damaging therapies (that require p53 to work) are commonly used in breast cancer and there is no standardised test that predicts whether p53 is working. The aim of this fellowship was to develop a “p53 test” to determine whether this pathway is functional in breast cancer.

I cannot describe what this funding has meant to me. At the beginning of 2018 the prospects for this project were not looking good. Without further funding more than 10 years of research would have come to an end and I would have needed to look for other career opportunities.

Thanks to this fellowship, I was able to continue my research and have been successful in obtaining two highly competitive external fellowships, providing job security for the next three years. I will finally be able to move towards translating these findings to a clinical test.

My overall goal is to incorporate p53 and its isoforms as a predictive test to aid treatment decisions in routine clinical practice. Firstly, it is imperative that we validate our findings in a clinical trial of a large number of patients whose outcome is known. Validation of our results will provide an essential first step in translating these findings to the clinic where we anticipate that p53 isoforms will be used to aid treatment decisions in breast cancer.

We believe that using this test to determine which treatment a patient should receive will significantly reduce the development of recurrences and secondary cancers and will improve survival from breast cancer.
SUMMARY OF FINDINGS

This fellowship provided an incredible opportunity to rapidly accelerate my academic outputs in 2018. With this generous support, I was able to submit two successful grant applications. The combined value of these two grants essentially doubled the amount of research income I have generated in the last three years.

I was also invited to two international speaking opportunities at the University of Calgary (July) and the International Psychos Oncology Society (October). As a direct result of these visits, I have strengthened new collaborations with internationally renowned leaders in my field such as Prof Joost Dekkers, Prof Barry Bultz, and A/Prof Fiona Schulte.

Finally and most importantly, I was recently awarded a highly-competitive three year fellowship which supports my salary and project costs for an innovative implementation trial to promote evidence-based cancer care nationally. This project will start in 2019 and will enable me to develop an independent research portfolio while guided by my mentors, Prof Chris Paul, Prof Barry Bultz and Dr Nicole Rankin.

I see my research career moving towards highly-collaborative, implementation trials. I believe I now have a strong competitive advantage as an early-career researcher. I am deeply thankful for this philanthropic investment in my career. It provided not just the resources to continue my research projects in 2018, but the track record and encouragement needed to be successful for my 2019 Fellowship application.

Dr Elizabeth Fradgley
Research Project Title: Unpacking the components of multidisciplinary cancer care in NSW: a mixed methods study to identify and develop efficient, patient-centred operating principles, referral protocols, and communication tools for team meetings.

STUDY 1: PATIENT-CENTRED DISTRESS SCREENING OPERATING PRINCIPLES
Although critical gaps across all guideline components were reported in this study, there is a broad support for screening and willingness to improve. Potential improvements include additional services to manage problems identified by screening, more staff time for screening, additional staff training, and use of patient-report measures. A manuscript is currently under review at Supportive Care in Cancer and was presented in two symposiums at an international conference. The study also provided preliminary data for a successful fellowship application.

STUDY 2: PATIENT-CENTRED REFERRAL PROTOCOLS
The START trial will be the first to rigorously test the effectiveness of an evidence-based structured approach in reducing callers’ distress levels and increasing access to supportive care services. To date, over 1000 distressed cancer patients and caregivers have participated. Data collection will end in December 2019. The data will be used by Cancer Councils to determine the cost and utility of the structured care pathway.

By leading components of this study, I was co-awarded the HCRA Engagement Award in 2018. A protocol paper is currently under review for publication in the Journal of Medical Internet Research.

STUDY 3: PHYSICIANS’ PERSPECTIVES OF REFERRAL PROTOCOLS AND COMMUNICATION
To date, we have compiled a sampling frame of over 110 clinicians in NSW and commenced recruitment in January 2019. The project has received ethics approvals and the interview guide has been pilot-tested.

STUDY 4: PATIENTS’ PERSPECTIVES OF REFERRAL PROTOCOLS TOOLS FOR TEAM MEETINGS
To date, we have received ethical approval and improved the study protocol to recruit VisionTree participants and provide locally-relevant data on this Local Health District initiative. The project commenced recruitment in January 2019.

OUTPUTS achieved as part of this fellowship

- Two National and three international presentations
- Local, state, international and community collaborations
- Five journal articles published
- One engagement award received
- Two highly competitive external fellowships obtained totalling $817,500
- One PhD student involved
SUMMARY OF FINDINGS

Ovarian cancer disproportionately accounts for more than half of gynaecological cancer-related deaths. It generally presents at an advanced stage and has poor outcomes even after chemotherapy treatment. Platinum chemotherapy resistance still occurs at high rates, which may be due to DNA repair defects yet to be fully characterized. Deficiencies in one DNA repair pathway may be compensated for by increased expression of another DNA repair pathway, resulting in platinum therapy or PARP-inhibitor chemoresistance. One approach to overcome this limitation is to find ways to prevent chemoresistance. This may be achieved by knowing the DNA repair profile of each patient that will lead to selection of patients that will respond to alternative novel and repurposed cancer treatments. This study will ensure that every patient diagnosed with ovarian cancer will be offered personalised and effective treatments based on their DNA repair profile.

FINDINGS TO DATE

Ovarian cancer cells were shown to undergo more apoptosis and cell death, and reduced cell proliferation, when treated with platinum chemotherapy combined with DNA repair inhibitors. The study is still in the preliminary stages and no conclusions have been drawn. This study will continue into 2019.

OUTPUTS

achieved as part of this fellowship

1
ONE LOCAL PRESENTATION

2
ATTENDANCE AT MULTI-DISCIPLINARY TEAM MEETING AND ENGAGEMENT WITH COMMUNITY MEMBER

1
RADIO INTERVIEW TO PROMOTE WORLD OVARIAN CANCER DAY

1
MAJOR FUNDING OBTAINED FROM PHARMACEUTICAL COMPANY
SUMMARY OF FINDINGS

The nervous system has long been known to play a critical role in the spread of cancer. Tumour cells can invade surrounding nerves and travel along them, seeding themselves in new and distant sites. That’s why, as cancers become more aggressive they metastasise. Nerve infiltration also promotes cancer related pain. However, little is known about how nerves and cancer cells talk to each other. This proposed project focuses on revealing the interaction between nerves and tumours and how to block cancer-related pain signals.

Successful completion of this fellowship will advance our understanding of cancer management.

The majority of cancer patients suffer neuropathic pain during treatment. Based on previous research, we know that most cancer treatment strategies lead to induction of a stress condition in cancer. What is the role of cancer stress in the nervous system? Does the stress condition lead to cancer related pain?

With the support of this fellowship, we have found that tumour ER stress can be transmitted to neuron cells within the tumour micro-environment, which promotes neuron outgrowth. This was the first study to link tumour cells and neurons in a new functional interplay that underscores the tumour cells effect to seize control of neuronal cells in the microenvironment and the whole nervous system, ostensibly leading to tumour growth and progression. This study also revealed that tumour ER stress contributes to cancer related neuropathic pain.

Understanding the effect of ER stress on the generation and maintenance of cancer pain opens routes to exploit this system for therapeutic purposes and assist in increasing cancer patients’ quality of life.

Therefore, this new project not only focuses on basic science but also provides more information in improving cancer patients’ quality of life.

This fellowship has allowed me to generate a large body of preliminary data in a new research area. This research is a continuation of my previous work, but has been expanded into a much wider area of translational study. The data I have generated during this fellowship will be valuable in contributing to grant applications this year.

I have been working on cancer signal transduction since I completed my PhD, however, only a small proportion of signal transduction studies can be translated into a clinical setting.

This new project not only focuses on basic science but also provides more information in improving cancer patients’ quality of life.

Although I was not successful in receiving an external fellowship in 2019, the data I was able to gather during my Career Advancement Fellowship in Cancer Research will be a huge contribution to my future grant applications.