Cancer Council Victoria

Prostate Cancer Research

Newsletter | April 2017

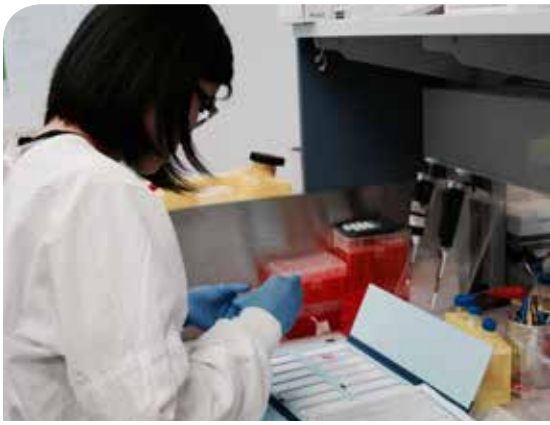
Study of Lifestyle and Genetic Risk factors for Prostate Cancer

After much research, what can be done to prevent prostate cancer remains poorly understood because, although the scientific literature on the subject is large, the evidence remains weak and inconsistent. Part of the reason for this is that prostate cancer is very common, almost all men will develop some form of cancer in their prostate in their lifetime, yet only a minority will develop a cancer that will go on to kill. It is the latter that we wish to prevent but historically the majority of study participants have been diagnosed with small slow growing tumours that are unlikely to kill – tumours that men tend to die with, not from.

In our case-control study we focus on men whose prostate tumours are more likely to spread and kill and compare them with men of similar age who underwent medical investigation for prostate cancer but after biopsy were found to be free of cancer. It has taken us 5 years to recruit 1518 cases and 1255 controls. This is a smaller number and a longer time than we had expected but this reflects a downward social trend in research participation, with men participating less frequently than women. Nevertheless, we have a relatively large study for which the data have been cleaned and prepared for analysis. Nathan Papa is analysing the data collected on aspects of lifestyle for his PhD thesis and findings should be published over the next 18 months or so.

In parallel to this work, our plans for genomic analysis include a genome wide association study that will measure ~500,000 common genetic variants across the entire genome. These data will make a substantial contribution to the ongoing search for common genetic variants associated with aggressive forms of prostate cancer. They will also be used to develop risk prediction models that will combine conventional risk factor information such as advancing age, family history of prostate cancer or ethnicity, with genetic variant information to classify men according to their risk of developing aggressive prostate cancer. Accurate risk prediction models could be of enormous value in identifying the minority of men who stand to benefit from screening and early detection and the majority who do not require these interventions. Our senior research fellow Dr Robert MacInnis is leading this work.

Additionally, we have joined an international collaboration led by Dr Chris Haiman at the University of Southern California who will use our DNA samples for whole exome sequencing. This is an efficient way to identify, for every gene in the genome, rare variants that cause differences in protein coding that may lead to disease such as prostate cancer. This is a very large study to which we will contribute about 20% of the DNAs. While cheaper than whole genome sequencing, whole exome sequencing is still relatively expensive and the costs will be borne by funding provided by the US National Cancer Institute. We will contribute DNA samples for sequencing from all men who have participated in one of our prostate cancer studies (including Health 2020 and the Australian Prostate Cancer Family Study) who meet the inclusion criteria for a case or control specified by Dr Haiman's scientific protocol. The genotyping will be done in 2017 and scientific reports are likely to be published in 2018.



Prostate tumour tissue is examined at our research laboratory.

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Our work on retrieving prostate cancer tissue samples for research

A very important aspect of our research into prostate cancer involves studying prostate cancer tissues.

Prostate tissue is frequently removed to help make a prostate cancer diagnosis and to help make decisions about the best treatment options for each man found to have the disease. Sometimes the whole prostate is removed as part of the treatment plan. This tissue is preserved and stored by the pathology service that makes the cancer diagnosis, usually for many years. Most men participating in our studies have been very generous and allowed us to access this material for further research. Many of the diagnostic laboratories that hold this material are supporting our research by providing this tumour tissue (that is left over from making the diagnosis) to our research program. In recent years our research team has worked very hard to communicate with pathology services and to collect the tumour tissue from across Australia that has been diagnosed in participants.

The laboratory based research team has also developed methods that now enable us to test this tumour tissue using new "high density" genomic platforms that have revolutionised cancer research. Our team can now examine the entire genome of a cancer in a single analysis using DNA extracted from these small amounts of tumour tissue and this work is advancing our understanding of what drives prostate cancer development and therefore what might prevent it.

How is your data being used?

Below is a selection of scientific papers that have been recently published using data from the Prostate Cancer Research Program. Some of this research has involved researchers from across Australia and around the world.

Al Olama, A. A., Z. Kote-Jarai, S. I. Berndt, et al. A meta-analysis of 87,040 individuals identifies 23 new susceptibility loci for prostate cancer. Nat Genet. 2014 46(10): 1103-1109.

Amin Al Olama, A., Z. Kote-Jarai, F. R. Schumacher, et al. A meta-analysis of genome-wide association studies to identify prostate cancer susceptibility loci associated with aggressive and non-aggressive disease. Hum Mol Genet. 2013 22(2): 408-415.

Eeles, R. A., A. A. Olama, S. Benlloch, et al. Identification of 23 new prostate cancer susceptibility loci using the iCOGS custom genotyping array. Nat Genet. 2013 45(4): 385-391.

MacInnis, R. J., D. F. Schmidt, E. Makalic, et al. Use of a novel non-parametric version of DEPTH to identify genomic regions associated with prostate cancer risk. Cancer Epidemiol Biomarkers Prev. 2016.

MacInnis, R. J., G. Severi, L. Baglietto, et al. Population-Based Estimate of Prostate Cancer Risk for Carriers of the HOXB13 Missense Mutation G84E. PLoS One. 2013 8(2): e54727.

Severi, G., L. M. FitzGerald, D. C. Muller, et al. A three-protein biomarker panel assessed in diagnostic tissue predicts death from prostate cancer for men with localized disease. Cancer Med. 2014 3(5): 1266-1274.