



## Review of the ninth Cancer Research Workshop

The themes of the ninth C4 Cancer Research Workshop were familial cancer and new advances in using immunotherapy against cancer. Both areas have had media publicity over the last year, and are areas of great research interest here in Christchurch.

The workshop was commenced by Iranui Stirling describing her family's history of cancer, and how people started to realise there might be a mutated gene underlying the increased risk. She described how her brothers and sister buried several family members over quite a short time frame about 25 years ago, and how a new cancer diagnosis in one of their children (now a third generation) sparked a search for the cause. The family has members who inherited a mutated CDH1 gene, which has also been found mutated in other New Zealand families with inherited diffuse gastric cancer. This mutation also brings a risk of breast cancer.

Iranui was followed by Jan Sullivan, a Senior Genetic Associate with Genetic Health Service NZ based in Christchurch Hospital. She described how with Next Generation Sequencing, they can explore mutations in many different genes in the same test. A panel of a number of genes is now tested for breast cancer in families. The problem is in understanding whether changes found are relevant. It is still important to choose which genes you want to look at. In other words, the family history remains very important in determining the best genes to tests and the relevance of any findings. More is not necessarily better.

Dr Logan Walker talked about BRCA1 which is one of the two most common genes to have mutations in familial breast cancer. Its role in cells is to help repair damage to DNA, so when it is mutated the cells can have large numbers of mutations due to poorer ability to repair mistakes. It has now been found that the new immune therapies have greatest success when there is a high number of mutations in the cancer cells. Logan also reported progress on gathering families who have breast cancer, and studying their DNA and searching for mutations, including previously unknown BRCA1 changes. The challenge is to correctly identify which mutations in breast (or ovarian) tumours may be associated with a positive response to these immune therapies.

The second half of the workshop offered more detail around the immune checkpoint inhibitors.

Associate Professor Margaret Currie described the way cancer cells use a number of surface receptors to evade the host immune system, and key among them is the Programmed Death Ligand receptor 1, known as PDL-1. A number of blocking agents are being developed by pharmaceutical companies. She showed how blocking this receptor enables the immune system to detect the cancer cell antigens and mount an immune response. However, not all people treated show response, and serious side effects occur in some patients. With PhD student Leah Butt and Dr Matthew Strother, she is measuring aspects of the immune response in patients with melanoma who are receiving immune therapy.

Dr Strother, one of the Christchurch Hospital oncologists, described the effects of immune therapies for melanoma, from the very earliest (but very toxic) interleukin therapy, through ipilimumab, which binds to CTLA4, one of the other receptors preventing the immune system from reacting against cancer cells, to PDL-1 inhibitors. Pembrolizumab and nivolumab are both funded in New Zealand for advanced melanoma, but not for other stages of melanoma or other cancers.

Dr Dean Harris, oncologist, described the development of immune therapy for lung cancer. Results have shown benefits, but it remains unclear whether the level of PDL-1 in the cancer cells predicts for a good response, despite being specified in clinical trials. The Oncology Service has participated in a number of clinical trials to explore efficacy and safety of newly developing immunotherapies, in several cancer types.

The C4 thanks the speakers for giving up their time, and preparing such clear presentations, and the Mackenzie Cancer Research group members for the refreshments, and Associate Professor Gabi Dachs for bringing the programme together. The Mackenzie Cancer Research Group acknowledges their support from the Mackenzie Charitable Foundation.

## The C4 brainstorms for the future of cancer care in Canterbury

Members of C4 met recently to brainstorm what future cancer services in our region could look like. We had a good mix of clinicians, supporting NGOs, and researchers attend.

We wanted a centre of excellence for cancer care in the upper part of the South Island, and to centralise the initial diagnostic processes and the decision-making, but aim to deliver anticancer treatments and supportive care closer to home. This would be a "hub and spoke" model.

In addition, it was a strong recommendation that research should be integrated into every stage of the patient journey, so we aim for continual increase in knowledge and better care. However, we need input from consumers and primary care, and this is just one of a number of discussions over coming months. The outcome will inform future physical building for the cancer services as well as how they function, in partnership with the University of Otago and other academic institutes, primary care and the community.