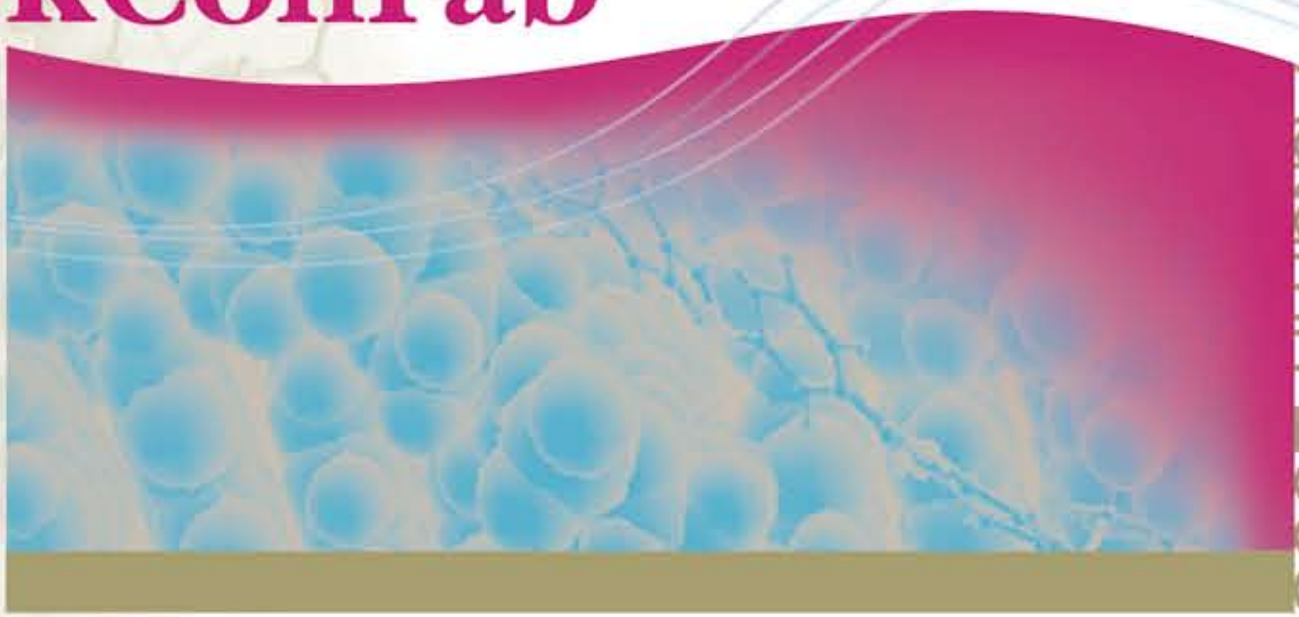
kConFab



Autumn 2008

DEAR READERS

Australian researchers and clinicians became very excited a few months ago about the discovery of five new genes that increase the risk of breast cancer. The work was carried out by a large consortium of international researchers, led by Douglas Easton and his colleagues in Cambridge UK, who used data and DNA samples collected from women in many countries. Australia was well represented. My research group at the Queensland Institute of Medical Research, Professor John Hopper from the University of Melbourne and Professor David Bowtell from the Peter MacCallum Cancer Centre (using data and biological samples collected by kConFab, the Australian Breast Cancer Family Study and Australian Ovarian Cancer Study) all contributed to this international effort.

What are the new findings?

We have known for many years about the two major breast cancer genes - BRCA1 and BRCA2. About 30% of families with many cases of breast and ovarian cancer carry mutations in one or other of these genes. But what causes cancer in the rest of the families? Douglas Easton and colleagues in Cambridge decided to search the human genome for genes that were not as powerful as BRCA1 or BRCA2 but could nevertheless contribute to cancer. Because of knowledge and techniques that have come from the Human Genome Project, Doug Easton could compare the genomes of cancer patients with those of people without cancer. They identified many genes that were different in the two groups.

Further work showed that these genes individually carry only a small risk of breast cancer. But the risks add up and become very significant in women that happen to inherit changes in several of these genes.

Some of these genes have been known for years, but until now were not suspected of being involved in familial breast cancer. Because they each contribute only a relatively small risk of disease, they are known as polygenes and have individual names such as FGFR2, TNRC9, MAP3K1, LSP1 and CASP8. Researchers in kConFab who are part of this international research investigation are planning experiments to look at the biological and clinical implication of changes in these new polygenes. We hope that within a few years a test will be developed to identify women in the population at the highest risk of breast cancer (regardless of their family history) and offer more intensive screening to detect breast tumours early.

We have added a reminder on page 5 about contacting us if you are having surgery, as we are still keen to collect donations of all types of tissue.

Finally, a big-thank you to all kConFab participants and family members who donated art work for the Friends of kConFab "Breast Cheque" art show which was held at The Menzies art brand gallery South Yarra, in September 2007. We have a story about this event on page 5 but your generous support was greatly appreciated by the whole kConFab team. An amazing $80,000 was raised. It was a privilege to see how gifted you all are and how important art is to so many of you.

Yours sincerely

Georgia Chenevix-Trench
Chair, kConFab Executive committee

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Research into FAmilial Breast Cancer
Kathleen Cuningham Foundation
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RESEARCH UPDATES

Faults (mutations) in the breast cancer gene BRCA2 can cause prostate cancer in men

kConFab researchers based at The Peter MacCallum Cancer Hospital and The University of Melbourne have demonstrated for the first time that mutations in the BRCA2 gene are directly responsible for most of the prostate cancers that arise in male mutation carriers. However, there did not appear to be an association between mutations in BRCA1 and the development of prostate cancer.

This kConFab study demonstrates the importance of men's family cancer history, especially if they belong to a family with a known BRCA2 mutation and have cases of breast and/or ovarian cancer. Future research may provide evidence to support intensified screening of men at increased genetic risk of prostate (please see IMPACT the article directly below).

The title and contributing authors of this work to be published soon in the American Cancer Research journal is:

Loss of heterozygosity at the BRCA2 locus detected by MLPA is common in prostate cancers from men with a germline BRCA2 mutation. Amber J. Willems[1], Sarah-Jane Dawson[2], Hema Samaratunga[3], Alessandro De Luca[4], Yoland C. Antill[2], kConFab Investigators[1], John L. Hopper[5], and Heather J. Thorne[1].

Kathleen Cuningham Consortium for Research into Familial Breast Cancer (kConFab), Research Department Peter MacCallum Cancer Centre, Locked Bag 1, A'Beckett St, Victoria, Australia; [2] Department of Haematology and Medical Oncology, Peter MacCallum Cancer Centre, Locked Bag 1, A'Beckett St, Victoria, Australia; [3] Department of Anatomical Pathology, Sullivan Nicolaides Pathology, 134 Whitmore Street, Taringa, Queensland; Australia, [4] Centre for Translational and Applied Genomics, British Columbia Cancer Agency, Vancouver, BC, Canada; [5] Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, School of Population Health, The University of Melbourne, Victoria, Australia.

IMPACT UPDATES

- (Identification of Men with a genetic predisposition to ProstAte Cancer: Targeted screening in BRCA1 and BRCA2 mutation carriers and controls)

Dr. Gillian Mitchell, Peter MacCallum Cancer Institute and Dr. Geoff Lindeman Royal Melbourne Hospital, Melbourne.

You may remember that in the last kConFab newsletter, we highlighted a study about prostate cancer screening that was about to start recruiting. It is called the IMPACT study and its full title is Identification of Men with a genetic predisposition to ProstAte Cancer: Targeted screening in BRCA1 and BRCA2 mutation carriers and controls.

This is an international study that was set up because men who are from families where there is a mutation (fault) in the BRCA1 or BRCA2 genes causing an increased risk of breast and/or ovarian cancer may be at increased risk of prostate cancer if they have inherited the same gene change. The risk of prostate cancer for men with the BRCA1 mutation are less than for men with a BRCA2 mutation.

This study is looking to see if yearly screening with a PSA blood test is a useful way to detect prostate cancer in men from these families. To answer this question, we are comparing the results of PSA tests in men who have been found to carry the family BRCA1 or BRCA2 mutation against the men who do not carry their family mutation. To take part in the study men have to be in a family where there is a known alteration the BRCA1 or BRCA2 gene. Men who are interested can take part whether or not they know their own genetic test result.

Participation in this study involves a yearly visit to a study hospital to complete a questionnaire and have a sample of blood and urine taken. If the PSA blood test is higher than the cut off level, then the man will be referred to a local urologist for further investigation. Subsequent treatment will depend on the results of the PSA test and any prostate biopsy done by the urologist.

We are now in a position to open the study throughout the country. So far we have opened the study at the Peter MacCallum Cancer Centre and Royal Melbourne Hospital in Victoria, through the South Australia Genetics service/ Repatriation Hospital in South Australia and Westmead Hospital in Sydney. We have so far recruited over 60 Australian men, which is over a third of the world-wide recruitment to date. **Two men have already been found to have early prostate cancer and have undergone the appropriate treatment for this.**

We will be writing to all the men in kConFab who are potentially eligible for the study inviting them to take part.

But if you are interested, you do not have to wait for the invitation and you can call Heather Thorne on 1800 221 894 or Melbourne 03 9656 1542 or email familial.cancer@petermac.org to register your interest at any time.

Upcoming Events:

Familial Cancer 2008: Research and Practice

A Combined meeting of kConFab, Australian Ovarian Cancer Study (AOCS), the Family Cancer Clinics of Australia and New Zealand

Venue:

Couran Cove Island Resort, Queensland

Dates:

19th – 22nd August 2008

Contact:

heather.thorne@petermac.org for further details or view the conference updates on the kConFab home page at http://www.kconfab.org

PARPI (PARP INHIBITOR) UPDATE

By Dr Clare Scott, Royal Melbourne Hospital and Dr Gillian Mitchell, The Peter MacCallum Cancer Centre, Melbourne.

We would like to give you a brief update about the treatment study targeting women with breast or ovarian cancer with a mutation in the BRCA1 or BRCA2 gene.

Last year we wrote a short article about a new drug, an inhibitor of an enzyme called PARP, in a tablet form that is now under investigation for women who have a BRCA1 or BRCA2 mutation and who have recurrent breast or ovarian cancer. The breast or ovarian cancers in these women are expected to be very vulnerable to this new type of chemotherapy (PARPi) because of the presence of the BRCA1 or BRCA2 mutation. **The study is available to women whose cancer has recurred and who require additional therapy.**

Two international clinical trials were opened last year, one for women with recurrent ovarian cancer and one for women with breast cancer. The ovarian cancer study opened and closed within a few months, as there were many women who were eligible for the study. In Australia we enrolled 20% of the women participating in the study worldwide. We are hoping that the results of the study will be very exciting and the early results will be presented at a large international conference in May this year. We will keep you updated about the results in the next edition of the newsletter.

The study for women with breast cancer is still open and available, **so if there is a member of your family who has a BRCA1 or BRCA2 mutation (fault) and has breast cancer that has returned and may need more treatment, then they may be able to take part in this trial.** If you or a member of your family is interested in hearing more about this trial, then please contact Heather Thorne on 1800 221 894 or Melbourne 03 9656 1542, who will put you in touch with the doctors running this trial.

Are there other genes that interact with BRCA1 and BRCA2 in the development of breast cancer? The answer appears to be YES.

By Dr Georgia Chenevix-Trench, Queensland Institute for Medical Research, Brisbane.

My laboratory is involved in a large international consortium know as CIMBA (Consortium of Investigators of Modifiers of BRCA1 and BRCA2). This group has pooled data on the lifestyle of almost 20,000 people from around the world (including participants from 1000 kConFab families), who are known to carry a BRCA1 or BRCA2 mutation. Our research has shown that changes in some of the polygenes identified by the Breast Cancer Association Consortium (see this edition's editorial), when present with a BRCA1 or BRCA2 mutation appear to increase the likelihood that breast cancer will develop. In the future, information of this type may help a women decide if and when she wants to have prophylactic surgery to reduce her risk of breast cancer.

AROUND THE CLINICS – UPDATES

Westmead Familial Cancer Service welcomes a new genetic counsellor, Michelle Howson to the team.

The Familial Cancer Registry of Western Australia currently has 517 registrants 214 who are included in the Registry for reasons related to breast cancer, with the remaining 303 being registered because of hereditary colon or other familial conditions. The Registry is a voluntary service that accepts people with known mutations or who are from families that require high -surveillance.

The Registry assists with managing surveillance by keeping records of reports and providing a reminder service to those whose surveillance is overdue. When a report is received, it is scrutinized and checked against personal and family history. As scientific progress is made or family circumstances change, surveillance recommendations may also change and members are notified.

Breast surveillance in Perth is well organised. Those with mutations (or those from high risk families) are seen annually in a high-risk, one-stop-shop clinic conducted across two major metropolitan teaching hospitals. These clinics offer specialist care and, if need be, access to imaging techniques such as MRI.

The Registry works in collaboration with the high risk clinics, Genetic Services of WA and kConFab to help provide personal, appropriate and timely services to those with an increased risk of breast cancer.

Pink Blush.....

In March 2007 Crystal, the daughter of one of our kConFab families, was married in a pink wedding gown to honour the three generations of women with breast cancer in her family. The gorgeous gown was perfectly matched in colour to the National Breast Cancer Foundations Pink Ribbon. Guest donated $2 into a beautiful pink beaded box that had been hand made by Crystal's mother Julie-Anne. The box contained a National Breast Cancer Foundation Pink Ribbon that was worn by all guests on the night. All proceeds raised were donated to the National Breast Cancer Foundation, who distributes funds Australia-wide to research projects like kConFab.

Crystal and Chris on her wedding day
Photograph generously provided by Jeremy Byrnes:
jeremy@jeremybyrnes.com www.jeremybyrnes.com

BOOK REVIEW:

Singing the Life – the story of a family in the shadow of cancer

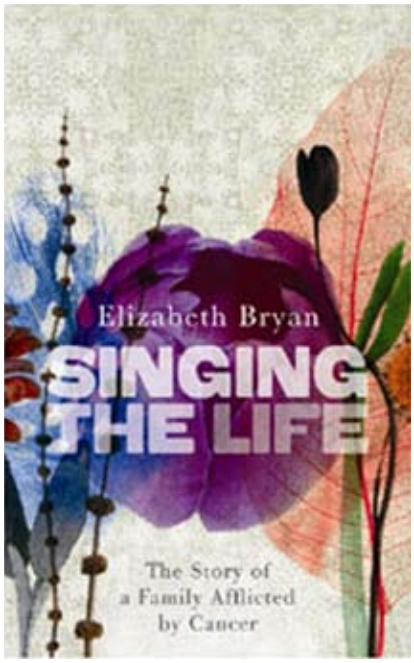
By Elizabeth Bryan; published by Vermilion

This title alone will probably strike some chords with kConFab participants, and the book is likely to be of interest to many. Elizabeth (Libby) Bryan has known since she received a letter out of the blue from a cousin in 1975 that her family had many cases of ovarian cancer. Even back then, the letter suggested that the women in the family might want to consider having their ovaries removed to reduce their risk of cancer, although the writer was not sure whether the susceptibility could be passed through a male, Libby's father.

For the next decade or so Libby was busy with her professional life as a very successful paediatrician and expert in multiple births, but her personal life was affected by her inability to have children. Her love of children is demonstrated by the many references to her 14 godchildren and 16 grand-godchildren. When Libby finally had her ovaries removed to reduce her cancer risk, after her sister was diagnosed with ovarian cancer, she felt a sense of relief. .

The first half of the book tells the moving story of her family since that letter in 1975, including one sister's death from ovarian cancer, another's development of breast cancer, her father's death from prostate cancer, the identification of a mutation in the BRCA1 gene in their family, and in Libby herself, and her own prophylactic oophorectomy and mastectomy. Libby describes her sister Bunny's death and the mixed reactions of everyone, particularly Bunny's young children, to the tragedy. Despite a professional lifetime of helping grieving parents, Libby found she was ill equipped to deal with such a personal experience in her young and traumatised nieces. She also discusses many of the practical issues around her mastectomy, and its 'minor' complications that did not seem so minor to her at the time.

By the time Libby was told that she herself was a carrier, having inherited the mutation from her father, she was so expecting the news that it came as little surprise - even though she knew before the test that she only had a 50% risk of carrying the mutation. What did come as a surprise, however, was her diagnosis of pancreatic cancer in 2005. Pancreatic cancer is not usually associated with BRCA1 mutations,



and still no one knows if her cancer was related to her BRCA1 mutation status, or just incidental. She realised immediately that the prognosis for this cancer is very poor, and so the implications very serious, and the second half of the book is much more reflective, as she describes her own surgery and chemotherapy, and thoughts about life and death.

Despite the content, and Libby's uncertain future, this book is funny and informative, as well as of course very sad in parts. Libby discusses the genetics of breast cancer in a very simple way, and leaves open many of the ethical issues, particularly about how to inform the younger members of the family about their risks and options. She also tries to put the cancers in her family into perspective, not least against the background of the bipolar disorder which also runs in her family and directly, or indirectly, claimed the lives of her mother and her niece. We recommend this book highly to anyone with a personal or professional interest in familial cancer.

Editors note: We write with great sadness to tell you that Libby passed away on Thursday, 21st February 2008. Despite some very happy times and superb medical care, she had been going gently downhill for some weeks and died peacefully at home as she had hoped, looking out at the Black Mountains. We extend our condolences to her family and close kConFab friends.

Available via Amazon or Random House Australia.

http://www.randomhouse.com.au/

Mothers Day Classic

The Mothers Day Classic will be held nationally on Sunday 11 May in capital cities and regional areas.

Last year, the Mothers Day Classic attracted more than 50,000 participants nationwide and raised over $800,000 for its beneficiary, the National Breast Cancer Foundation. The total raised by the event for breast cancer research since 1998 is more than $3 million.

Who organises the event?

The events are organised and presented by Women in Super - a national network of women working in the superannuation industry.

The vast majority of the people who help to put together the Mothers Day Classic are volunteers. They give their time each year as a way of actively contributing to the fight against breast cancer.

This initiative was inspired by the knowledge that research is gradually improving the survival rate of the one in 8 women who will be diagnosed with breast cancer during their life. Improving the quality of life of those with breast cancer is a valuable and rewarding investment into our community.

Where does the money raised go?

All proceeds from the Mothers Day Classic are donated to the National Breast Cancer Foundation, a not for profit organisation that promotes and supports research into breast cancer prevention and treatment.

How can I be involved?

In Brisbane, Melbourne, Adelaide, Hobart, Sydney, Perth, Canberra and regional areas you can participate in the Mothers Day Classic Walk and Run. It's a fun day for everyone involved with food, activities and kids entertainment available. You can enter as an individual, family or part of a team.

To register visit - www.mothersdayclassic.org

Messages from the kConFab team:

To keep kConFab running smoothly, we would greatly appreciate if you would remember the following:

- Because we send information to you by mail, it is very important to keep your contact details up to date.

  We may even ask you to send us the name of another contact person, in case we are unable to find you. Please use the toll free number to pass on these updates 1 800 221 894 and speak to Heather or ring your local kConFab research nurse to inform them of any surgery planned for treatment or prevention.

- Please remember that **fresh tissue specimens, normal and cancer of all tissue types, obtained at surgery** are extremely valuable for our research. In addition to the tissue collections, sometimes, in the course of breast or ovarian cancer, women experience the build up of fluid in their abdomen (this fluid is called ascites) or lungs (pleural effusion). The ovarian or breast cancer cells in these fluids can be used in our research studies. If you find yourself needing to have ascites or lung fluid drained at any time, we would greatly appreciate being contacted by either yourself or your medical staff in advance, so that we can arrange to collect any fluid not required for diagnostic use. Our team would make all the necessary arrangements.

- It is very important that we are notified of any new cases of cancer in your family. Research relies on accurate and up-to date information about the cancers in each of our participating families. We appreciate your help with this.

  • Please notify kConFab if, at any time, you prefer not to have more contact with our study

- Please tell your research nurse if you change your address

- **Are there other family members eligible to join kConFab?**

  - Once a family has been counselled at a Family Cancer Clinic about a genetic (fault) mutation in the family, additional family members may become eligible for recruitment into the kConFab study.

  - Once a family member, female and male turns 18 years of age they may also be eligible to be recruited into the kConFab study

  Please call one of our research nurses (see contact list at the end of this newsletter) if you would like to confirm if other family members are eligible for recruitment.

The friends of kConFab

"Breast Cheque" art show, September 2007

The Friends of kConFab main fundraising event for 2007, in partnership with the National Breast Cancer Foundation, was an art exhibition and auction in September as a lead up to Breast Cancer Month.

100% of all funds raised will be directed towards our national research efforts. We were very fortunate in securing the sensational ***Menzies art brand gallery*** from ***Rod and Carolyn Menzies***, Darling Street South Yarra, Melbourne for this event. kConFab wrote to many of our breast cancer survivors in Australia inviting any of our artists or art enthusiasts to consider donating an existing artwork (painting, photography, sculpture or glass work) for this exhibition and auction. In addition to art works, we also included brief stories in the exhibition catalogue demonstrating how art has helped women cope with a diagnosis of breast cancer or with breast cancer in the family. The response to our request was amazing. We had on display and for auction 120 art works from kConFab family members, clinicians and scientists.

Thank you to the Friends of kConFab for the work they put into organising this event, Rod and Carolyn Menzies for the donation of their gallery, access to their excellent staff and for the donation of art works from their personal collection for auction. Thanks also to ***media personality Ms Suzi Wilks*** for making the opening speech. Finally, there would not have been an art show without the generous donations of artwork, so a special thank you to all of the artists involved. We hope you enjoyed viewing your work in such a wonderful venue – we certainly did!

If you would like to hold a fundraising function for breast cancer research, please contact the kConFab office on **1 800 221 894** or **03 9656 1542** as we will be able to assist you with the organisation of your event and provide copies of the kConFab "Who's at Risk" information brochure that describes our national research work and how our funds are managed by the National Breast Cancer Foundation. **All** funds raised by the **Friends of kConFab** will be used for **research** so we can reach our **long-term goals**.

Collaborating Family Cancer Centres

Melbourne

Familial Cancer Centre
Peter MacCallum Cancer Institute
St Andrews Place
East Melbourne, 3002
Contact: Ms Mary-Anne Young
Phone: 03 9656 1199
kConFab research nurse: Tina Thorpe
Phone: 03 9656 1903

Royal Melbourne Hospital
Familial Cancer Centre
Parkville, 3050
Contact: Dr Geoffrey Lindeman
Phone: 03 9342 7151
kConFab research nurse: Tina Thorpe
Phone: 03 9342 4257

Victorian Clinical Genetics Service
Monash Medical Centre
Clayton
Contact: Dr Marion Harris
Phone: 03 9594 2026
kConFab research nurse: Tina Thorpe
Phone: 03 9656 1903

Sydney

Familial Cancer Service
Westmead Hospital
Westmead, 2145
Contact: Assoc. Prof. Judy Kirk
Phone: 02 9845 6947
kConFab research nurse: Rachel Sinclair
Phone: 02 9845 6845

Prince of Wales Hospital
Hereditary Cancer Clinic
High Street
Randwick, 2031
Contact: Dr Kathy Tucker
Phone: 02 9382 2577
kConFab research nurse: Helen Conlon
Phone: 02 9382 2607

St George Community Hospital
Hereditary Cancer Clinic
Kogarah, 2217
Contact: Dr Kathy Tucker
Phone: 02 9382 2577
kConFab research nurse: Helen Conlon
Phone: 02 9382 2607

St Vincent's Hospital
Family Cancer Clinic
Darlinghurst, 2010
Contact Dr Robyn Ward or Ms Rachel Williams
Phone: 02 8382 3395

The John Hunter Hospital
Hunter Valley, NSW
Contact: Dr Tracey Dudding
Phone: 02 4985 3132
KConFab research nurse: Helen Conlon
Phone: 02 9382 2607

Brisbane

Queensland Clinical Genetics Service
Royal Children's Hospital
Bramston Terrace
Herston, 4029
Contact: Dr Michael Gattas
Phone 07 3636 1686
kConFab research nurse: Vicki Fennelly or Allison Wicht
Phone : 07 3636 5200

Adelaide

South Australian Clinical Genetics Services
Women's and Children's Hospital
North Adelaide, 5006
Contact: Dr Graeme Suthers
Phone: 08 8161 6995
kConFab research nurse: Meryl Altree
Phone: 08 8161 6821

Perth

Genetic Services of Western Australia
King Edward Memorial Hospital
374 Bagot Road
Subiaco, 6008
Contact: Dr Ian Walpole or Professor Jack Goldblatt
Phone 08 9340 1525
kConFab research nurse: Anna Nash
Phone: 08 9340 1610

Tasmania

The Royal Hobart Hospital
The Launceston General Hospital
The North West Regional Hospital, Bernie
Contact: Dr Jo Burke
Royal Hobart Hospital
Phone: 03 6222 8296
kConFab research nurse: Tina Thorpe
Phone: 03 9656 1903

Auckland – New Zealand

Northern Regional Genetics Services
Auckland Hospital
Auckland, New Zealand
Phone 0800 476 123 ext 7232
Family Cancer Clinic Staff
NZ local call 0800 476 123, international 64 9 307 4949 EXT 5530

Wellington – New Zealand

Central and Southern Regional Genetics Services Wellington Hospital
Wellington South
Contact: Dr Alexa Kidd
Phone 64 4 385 5310
Phone International 64 9 307 4949 EXT 5530
NZ local call 0800 476 123

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