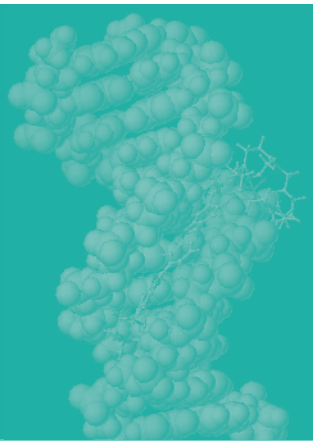
WINTER 2005 **NEWSLETTER**



kConFab

Kathleen Cuningham Foundation CONsortium for research into FAmilial Breast Cancer

Published by kConFab, Peter MacCallum Cancer Centre, St Andrews Place, East Melbourne 3002, phone (03) 9656 1542 www.kconfab.org

DEAR READERS,

There have been quite a few changes in kConFab in the last few months, the most important of which is that we have developed a new database that allows all the research nurses in Australia and New Zealand to submit their data in real time straight to the Peter MacCallum Cancer Centre in Melbourne.

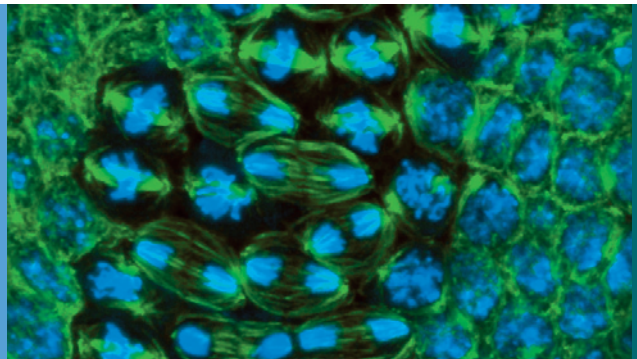
Now that we have data from more than 12,000 individuals, and blood specimens from almost 10,000 participants, management of the data and specimens has become a huge task and the Data Manager, Eveline Niedermayr, and the research nurses have done an excellent job converting to our new database.

The response to our new fridge magnets has been very helpful! Many women have phoned the toll-free number to notify us of changes in address, or impending surgery, or just to ask questions about kConFab. Please phone Heather Thorne a few days before surgery at 1800 221 894 if you would like to donate tissue to kConFab, so that she can make arrangements with the local surgeon and pathologist to collect the tissue at the time of the operation.

As we have mentioned before, this allows the tissue to be frozen which preserves it much better than the standard pathology storage protocols and these fresh tissue collections are the most important of all the material that kConFab collects. There are plans to use the freshly frozen tissue to identify new 'biomarkers' (indicators) that might be used in the future to detect breast cancers before there are any clinical or mammographic signs.

Nearly 1,000 families from all corners of Australia and New Zealand have now been recruited to kConFab, which is great for our research into familial breast cancer. But we are also very aware that this represents 1000 families who bear a heavy burden of this disease, and we are continually grateful for your willingness to help in research that we all hope will lead to better outcomes.

Sincerely,
Georgia Chenevix-Trench
Chair, kConFab Executive Committee



Editor's note: The following article was written by Dr. Peter Grant in response to many phone calls to the kConFab office for information on the effects of prophylactic oophorectomy (removal of normal ovaries) from pre-menopausal women.

MANAGING SYMPTOMS AFTER OOPHORECTOMY IN PRE-MENOPAUSAL WOMEN

left to right:
Dr Victoria Beshay, Research Scientist, Dr Marion Harris, Medical Oncologist and Mr Peter Grant, Surgeon.

The decision to remove the ovaries from a pre-menopausal woman is often daunting. Removing ovaries decreases her chances of developing breast and ovarian cancer but may also cause rapid onset of menopausal symptoms.

The ovaries produce oestrogen, progesterone and many other hormones and once they are removed the levels of these hormones fall rapidly, unlike the situation in natural menopause where hormone production decreases over many years.

The effect of removing these hormones varies enormously from one woman to another. There are some women who experience minimal menopausal symptoms while others have profound symptoms that require active treatment. Many fall somewhere between the extremes and a woman's decision to seek treatment for the acute menopausal symptoms is tempered by the knowledge that the symptoms will often improve over 1-2 years.

The most common symptoms that may occur after removing the ovaries are:

- Hot flushes
- Sleep disturbance
- Mood changes, poor concentration
- Headaches
- Musculo-skeletal discomfort, joint stiffness
- Altered sexual function – loss of libido, vaginal dryness

Some of the problems that may be accentuated by early menopause do not appear immediately but may have a significant impact on quality of life in later years.

These problems include:

- Bone loss – osteoporosis
- Altered bladder function
- Increased risk of cardiovascular disease

The most distressing and common acute menopausal symptom is the occurrence of hot flushes. The most effective treatment for this and most other menopausal symptoms is oestrogen replacement therapy, but there is uncertainty surrounding this treatment which makes it a difficult decision. Fortunately, there are non-hormonal alternatives that are effective for many women in overcoming hot flushes.

Black cohosh is an extract from root of *Actaea racemosa*. It is marketed under several proprietary names and is readily available It has been shown to improve hot flushes in 50-60% of women when taking 40-80 mg/day.

Vitamin E, taken at a dose of 800-1000 IU/day improves menopausal hot flushes in 50% of women. Other types of non-hormonal prescription medication may be helpful in controlling hot flushes, with the most effective being sertraline. About 50% of women will notice an improvement in symptom control with this medication.

Phyto-oestrogens are naturally-occurring oestrogens obtained from some grains, legumes and green leaf vegetables. While individuals may find them useful in improving hot flushes they have been no better than placebo in several randomized trials and their long term effects on breast tissue are not known.

Vaginal dryness and irritation may be improved by the use of simple lubricants such as vegetable oil or lubricating gels. For some women using vaginal oestrogen 2 – 3 times a week is an good alternative and is probably the most effective means of overcoming difficult symptoms but the effect of the topical oestrogen on the uterus, if it was not removed at surgery, needs to be considered. The use of vaginal oestrogen may also improve bladder function.

The longer term issues of premature menopause, particularly on bone structure, can be well managed without oestrogen. Measures such as regular weight-bearing exercise lasting more than 20 minutes a day, a sensible and adequate diet, including 1000-1500mg calcium/day and vitamin D, reduce the risk of osteoporosis. Because women who have had a premature menopause are at an increased risk of osteoporosis they should think about having a baseline bone density scan within 2-3 years of menopause. For those women at risk of significant osteoporosis, despite the measures above, there are other medications available that are at least as effective as oestrogen.

In summary, there are many options available for improving the symptoms experienced by some women going through premature menopause. Ask questions and be prepared to try several different approaches until you find one that works for you.

Peter Grant, Surgeon
Head of Gynaecology and Oncology Department
Mercy Hospital for Women, Melbourne.

MENOPAUSE AFTER CANCER (MSAC) CLINIC IN PERTH

In WA we have established a dedicated multidisciplinary clinic for women with menopausal symptoms after cancer (MSAC). Previous research has shown that breast cancer survivors have a wide variety of on going information needs as well as support, psychological, practical, and physical support. The MSAC Clinic aims to support these needs through the dedicated clinic and the development of a specialist support nurse role.

Multidisciplinary Care

The clinic operates an open referral system and women are referred by breast nurses, oncologists, gynaecologists and GPs. Patients are seen in the clinic by the clinical support nurse and a gynaecologist or GP with a special interest in menopause. Continuity of care is a priority and women are usually seen by the same doctor each visit.

All new patients are discussed at a monthly Multidisciplinary meeting which is attended by gynaecologists, a breast surgeon, a medical oncologist, an endocrinologist, a GP, a clinical psychologist and a dietician.

High Risk Women

The MSAC clinic can advise women undergoing removal of their ovaries due to high risk of ovarian and or breast cancer on the best way to manage their menopause symptoms.

Quality Of Life

Cancer treatments including chemotherapy and endocrine therapies, such as anti-estrogens, may cause periods to stop and can also cause the onset of hot flushes, night sweats, vaginal dryness and other symptoms. Sometimes at diagnosis of cancer pre existing hormone therapy (HT) is stopped.

For younger women, this is often a shock, as they may be many years away from undergoing natural menopause. Those women who were taking HT before their cancer diagnosis may also feel their menopausal symptoms coming back and need assistance to manage these.

Menopausal symptoms after cancer can cause women to feel, embarrassed and worried. Questions about sexual function, fertility and safety of available treatment can be addressed at this clinic.

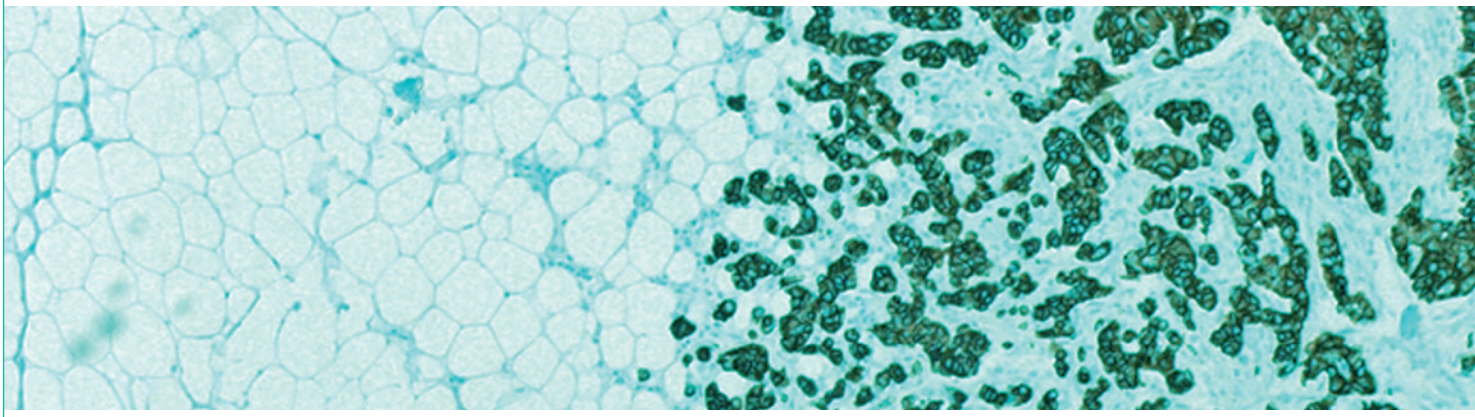
Treatment options

Conventional treatments such as Hormone therapy (HT) may not be appropriate because of concerns if the effects on breast cancer recurrence and other therapies may be effective and a better safety option.

Research

The Clinic is participating in research to assess the incidence and severity of menopausal symptoms in this population, the range of prescribed, non-prescribed and complementary therapies, and menopausal symptoms associated with anti-oestrogen treatments and chemotherapy compared to “natural” menopause.

Jane Gregson
MSAC Support Nurse
KEMH for Women
Bagot Road
Subiaco
Ph (08) 9340 2222
Page No 3358
Available : Tuesday and Wednesday



RESEARCH UPDATE

Dr Clare Scott and Dr Geoff Lindeman Medical Oncologist, RMH Familial Cancer Centre and research scientists The Walter & Eliza Hall Institute of Medical Research

"Mechanism-based" treatment of cancer:

Recent laboratory data have suggested that tumours lacking BRCA1 or BRCA2 proteins have faulty DNA repair processes and could be especially sensitive to chemo- therapeutic agents containing 'platinum salts', such as Carboplatin.

The issue will be addressed in an international clinical study, known as the "BRCA Trial". The study is a first step towards personalising chemotherapy treatment for patients with BRCA mutations.

The purpose of this trial will be to assess whether there is evidence that Carboplatin is an active and safe therapy in women with metastatic breast cancer who are BRCA1 or 2 mutation carriers. This will be compared to standard treatment with Docetaxel in terms of toxicity, and response. Efforts are underway by kConFab and the Australian New Zealand Breast Cancer Trials Group to ensure that this study is available to Australian women.

In a second approach, an exciting new anti-cancer drug that targets a DNA repair molecule known as PARP is under intensive pre-clinical laboratory investigation.

For people with cancers due to a faulty BRCA1 or BRCA2 gene, "PARP-inhibitors" may one day represent a new approach to selective tumour targeting. This is because PARP-inhibitors target an important DNA repair process:

In normal cells, the BRCA1 or BRCA2 gene can go on to repair damaged DNA. However, if the BRCA1 or BRCA2 gene is missing or faulty, DNA cannot be repaired properly and the cancer cell is forced to die. It is hoped that this drug might be safe to use because tumour cells lacking BRCA1 or BRCA2 should be more sensitive than normal tissue (which contains close to normal amounts of BRCA1 or BRCA2). However, the safety and efficacy of giving this drug to people with a faulty BRCA1 or BRCA2 gene has not been assessed.

These initial findings, published by two overseas groups in the prestigious scientific journal *Nature*, were made by studying cancer cell lines and using mouse models of cancer development.

It is likely that the human form of the disease may be more complex. Nevertheless, the research does offer an exciting new approach to be explored for treatment of people with faulty BRCA1 or BRCA2 genes.

It will take several years to evaluate PARP inhibitors through clinical studies in humans, which have yet to be initiated overseas or in Australia.

Prostate Cancer in kConFab Families:

Sarah-Jane Dawson, Medical Registrar and Yoland Antill, Medical Oncologist, Research Department and Family Cancer Clinic, Peter MacCallum Cancer Centre, Melbourne; and Professor John Hopper, University of Melbourne

Prostate cancer is the most common cancer affecting men, but the risks of developing the disease vary among the male population.

One of the risk factors for the development of disease is family history. We want to find out whether mutations in DNA repair genes such as BRCA1 and 2 increase the risk of not only breast and ovarian cancer but also prostate cancer.

The kConFab collection of breast/ovarian families, with its rich store of epidemiological, genetic and clinical data and matching DNAs, is the best resource worldwide to measure the risk of prostate cancer in these high-risk breast cancer families.

Knowing whether men who carry a BRCA1 or BRCA2 gene fault are at higher risk of developing prostate cancer could lead to improved screening and treatment in this population.

left to right: Dr Geoff Lindeman, Medical Oncologist and Dr Melissa Brown, Research Scientist.

left to right: Dr Gillian Mitchell, Medical Oncologist, and Dr Anna Tucker, Medical Oncologist, Research Scientist.

Banking on cancer research:

New support for tissue banking from Victoria, New South Wales and Queensland

Cancer and normal tissue that is removed from patients during surgery is always evaluated by a pathologist. Any remaining tissue, which is excess to diagnostic requirements, is usually discarded. This represents a lost opportunity for cancer research, which is increasingly dependent on studying tumour and normal tissue from patients.

Research on these samples represents a key means to identify the underlying genetic (and other) factors that lead to cancer and to develop new treatment strategies. Fortunately some kConFab participants who undergo cancer surgery or prophylactic removal of tissue (breast or ovary) have already been involved in donating their tissues to cancer research.

Exciting new initiatives to "bank" cancer and associated normal tissues for ethically approved research were recently funded by the Victorian, New South Wales and the Queensland Governments.

Most of these new initiatives are planning to collect and store tissues using methods pioneered in Australia by kConFab, However, the new tissue banking groups will collect a wide range of tissues and will not concentrate on cancers that occur in high risk families.

kConFab has a good working relationship with all of the new tissue banking groups which mean that collaboration and sharing of technical ideas will enhance all of the existing tissue banks.

kConFab participants who are about to undergo surgery may wish to discuss tissue banking options with their surgeon and kConFab nurse.

FIELD OF WOMEN - LIVE IN 2005

We did it!

The Field of Women – Live in 2005 at the Melbourne Cricket Ground was simply amazing.

11,500 women and 100 men brought the breast cancer statistics to life in a powerful and stunning visual display.

Visit our website www.bcna.org.au to see photos and read people's reactions to this event. 1800 500 258

THE "MY JOURNEY KIT" REQUEST LINE –

1 300 785 562

The My Journey Kit is available free of charge to those diagnosed with breast cancer in the last 12 months.

Gerda Evans
BCNA State Representative (Vic)
kConFab Community Representative
gerda@bigpond.net.au

SCREENING IN HIGH RISK WOMEN FOR BREAST CANCER – SHOULD I ASK FOR AN MRI?

Christobel Saunders, Breast Surgeon, QE11 Hospital, Perth

For women found to be at high risk for breast cancer, either because of a known family mutation (BRCA1 or 2) or because of their family history (ie. multiple cases of breast and ovarian cancer), the choice between intensive screening and prophylactic surgery is a hard one, made even more difficult because we know that the accuracy of current screening methods is nowhere near 100%.

So what screening tests are available to women at the moment and how effective are they in picking up breast cancers early and preventing women dying from the disease?

In Australia, BreastScreen offers mammographic screening to all women over 40 every two years, and we know that for women at "average" life-time risk of breast cancer this gives a 30% reduction in death from the disease. Many states will offer a mammogram every year to women with a family history.

However for young women (under fifty) at high risk there are a number of factors which make mammograms less effective:

- dense breasts make it difficult to see abnormalities on mammogram
- tumours in young high risk women breast cancers are often fast growing hich means that they can appear between mammograms.
- Even clinical examination in young women can be difficult, as can breast self examination.

Even more concerning is the possible risks of mammography in very young women:

- increased biopsy rates – for what turn out to be benign breast changes (some of which will mean unnecessary surgery)
- excessive radiation exposure in very young women putting them at increased risk of future cancers. It has been calculated that in very young women (under 35) 4 excess cancers occur for each 10,000 women having a mammogram every two years.
- BRCA1/2 mutation carriers and women having more frequent mammograms may be at even higher risk from radiation.

Many Familial Breast Clinics and individual clinicians recommend a surveillance program for young women at high risk which includes not only an annual screening mammogram, but also six-monthly clinical examination and annual breast ultrasound.

Because of all of the difficulties outlined above breast MRI has been explored over the last 10 years. MRI is a technique that avoids radiation exposure by using high strength magnets. It is highly sensitive at detecting breast cancer, even in women with dense breasts. It involves a test taking about an hour in which the woman has an intravenous injection of a "contrast" drug and then lies face down on a bed with her breasts in cups while the machine moves over the woman taking images of her breast and recording data about blood flow in the breasts.

The test is usually carried out about the same time as a mammogram, ultrasound and clinical breast examination as the information from all need to be put together. Although MRI is very sensitive, it cannot always discriminate between cancers and benign lesions. Moreover, as yet, very few radiologists in Australia have expertise in this technique, which is often hard to interpret, meaning that many women will need to have follow up tests including biopsy or surgery for abnormalities which turn out to be benign.

Also important is that this test does not yet have a Medicare Item number in Australia, so can only be done either as part of a funded research project or if the patient pays – with a cost of between $400 and $1000.

Despite all the above problems, there is a growing and very impressive body of evidence published in the literature which confirms MRI is the single most sensitive test for breast cancer in very high risk young women, often picking up cancers at an early stage when small and confined to the breast. However it needs to be done by an experienced team, as part of a surveillance programme.

So the answer to the question "should I ask for an MRI?" is: it should ONLY be done through a specialist breast cancer high risk clinic who will do it as part of a screening programme. The results from these programmes will help answer questions such as whether this test will increase survival for women at high risk of breast cancer

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.
- Sometimes we need to contact family members when a gene fault has been identified that is relevant for your entire family. In this case, we write notification letters to **all** family members who have indicated a wish to be informed about results of genetic testing for the family. We do not supply individual results, but instead suggest that family members should contact a Family Cancer Clinic, who can make the appropriate arrangements.

We understand that some family members may already know their own genetic testing results, having attended a Family Cancer Clinic. However, we know that others will not yet have been to such a clinic. The notification letter will provide details so that all of those who want a clinical genetic test can do so with the support of a Family Cancer Clinic. Some family members may have told us that they do not wish to be notified if kConFab finds a gene mutation in their family. These people will not receive a letter.

- Please remember that fresh tissue specimens obtained at surgery are extremely valuable for research. Please ring your local kConFab research nurse to inform them of any surgery planned for treatment or prevention,
- 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

How can interested families join kConFab?

Ring any of the research nurses or the kConFab manager listed below, or, view our home page to determine if your family meets our selection criteria:

http://www.kconfab.org/epidemiology/1eligibility.asp

NEW BREAST CANCER PATHOLOGY RESEARCH GROUP AT THE UNIVERSITY OF QUEENSLAND

Sunil R Lakhani Head,
Molecular and Cellular Pathology
The University of Queensland

We are pleased to welcome a new member to the kConFab Executive Committee. Professor Sunil Lakhani is very well known in the area of familial breast cancer research for his work in recognising that cancers from BRCA1 mutation carriers often have a distinctive appearance down the microscope.

For this reason we invited Sunil to the 2nd kConFab conference at Couran Cove in 2003, and he liked it so much that he moved his family and laboratory from London to Brisbane at the end of 2004, and took up the Chair of Pathology at the University of Queensland.

Sunil's laboratory has many projects aimed at understanding how breast cancers arise, but in particular the group is interested in the pathology and molecular pathology of familial breast cancers seen in patients with mutations in BRCA1 or BRCA2 genes.

Pathology is the study of the mechanism of disease and molecular pathology uses cell shape as well as a suite of laboratory techniques to understand the disease process. This helps pathologists make an accurate diagnosis, which in turn enables appropriate patient management.

Their work is now being translated to clinical practice to identify high-risk women whose cancers may have been caused by mutations in one of these genes. The laboratory is already working with other kConFab researchers to help to determine which variants of BRCA1 and BRCA2 are disease-causing, and which are just benign variants of no clinical importance, and also to try to develop new markers that might one day be used to identify cancers before they are detectable by mammography.

UPCOMING EVENT

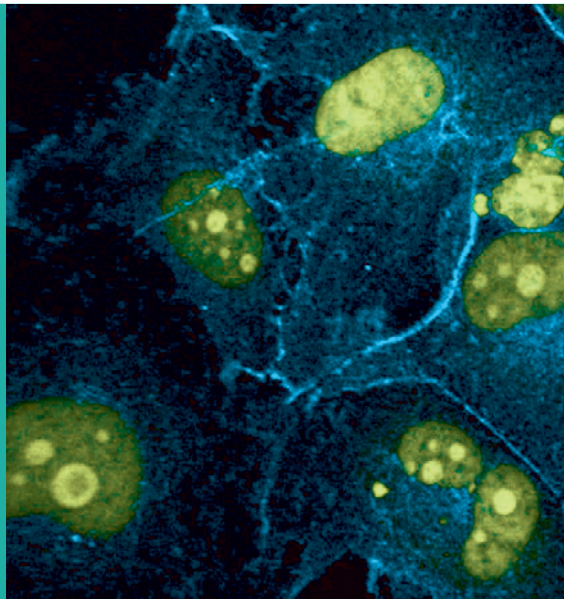
Familial Cancer 2005: Research and Practice

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

Venue: Couran Cove Island Resort, Queensland

Dates: Tuesday 30th August – Saturday 3rd September

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



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: Beth Spear
Phone: 03 9656 1903

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

Victorian Clinical Genetics Service
The Murdoch Institute
Royal Children's Hospital
Parkville
Contact: Dr Mac Gardner
Phone: 03 8341 6293
kConFab research nurse: Tina Saegi
Phone: 03 9342 4257

Victorian Clinical Genetics Service
Monash Medical Centre
Clayton
Contact: Ms Tarli Bogtstra
Phone: 03 9594 2026
kConFab research nurse: Beth Spear
Phone: 03 9656 1903

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

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 3253 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, or,
Susan Schulz 08 8161 6393

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 Lauceston General Hospital
The North West Regional Hospital,
Bernie
Contact: Dr David Amor
c/o VCGS Royal Children's
Hospital Melbourne, 3002
Phone: 03 8341 6300
or
Dr Jo Burke
Royal Hobart Hospital
Phone: 03 6222 8296
kConFab research nurse: Tina Saegi
Phone: 03 9342 4257

Auckland – New Zealand
Northern Regional
Genetics Services
Auckland Hospital
Auckland, New Zealand
Phone 0800 476 123 ext 7232
kConFab research nurse:
Jane Wylie
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
kConFab research nurse:
Jane Wylie
Phone International international
64 9 307 4949 EXT 5530
NZ local call 0800 476 123

kConFab Manager
Heather Thorne
Peter MacCallum Cancer Centre
Research Division
Phone: 03 9656 1542
Email: heather.thorne@petermac.org

USEFUL WWW SITES

KConFab – www.kconfab.org
National Breast Cancer Foundation – www.nbcf.org.au
Breast Cancer Network Australia – www.bcna.org.au
Breast Cancer Research Association Inc – www.breastcancer.asn.au