MAY 2004 **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
www.kconfab.org phone (03) 9656 1542

DEAR READERS,

We have decided that we should trial a six-monthly newsletter, instead of sending it annually. There are often issues we would like to communicate to kConFab participants, but the delay is too great if we do it via an annual newsletter. If there are any topics you would like us to cover in the newsletter, just let us know and we will do our best to include them.

One of the new directions for kConFab in the last six months has been the long-awaited match to information stored in the State Cancer Registries. As you probably know, all cancers are by law reported to these Registries, who use the data to follow changes in the incidence of the disease. kConFab has been trying for some time to match its data against the information in the registries but this has been a slow process because of the complex protocols required to obtain ethical approval from each separate State registry. We need to match our data against the registries a) to verify information about cancers in families, b) to locate pathology reports which provide a key to obtaining archival material from the Pathology Laboratories. Matching against registries guarantees that the information stored by kConFab for research is as accurate as possible.

In some States, data on cancers may take a year or more to appear in the registry. So to keep track of current events, if you, or any of your family members develop cancer, we would be most grateful if you could, at your convenience, notify your kConFab research nurse, or the clinical follow up team. As part of our annual follow-up, the kConFab nurses will also ask you whether new cancers have occurred in the family.

We have been very pleased with the response to our request for participants to notify us of impending breast or ovarian surgery. Several women telephoned us after receipt of our last newsletter to inform us that they were about to have surgery. This means that we have been able to collect fresh tissue directly from the surgeon and preserve it for future research projects. The material we collect from surgeons is extremely valuable for a large number of research projects – for example, to identify the very early stages that give rise to breast and ovarian cancers. We hope that this work will perhaps form the basis for novel therapeutic and prevention strategies. So, can I remind you again that if you are having prophylactic surgery, or surgery for a suspected malignancy, please contact your local kConFab research nurse and, with your agreement, she will make arrangements with the surgeon and pathologist to collect the tissue at time of surgery.

Last, but by no means least, thank you very much for your continued participation in kConFab. We could not exist without you and we very much appreciate the time and support that you commit to this long term research project. We have enormous co-operation not only from families and the Family Cancer Clinics but also from surgeons and pathologists who provide so much help to locate and deliver both fresh and stored specimens, and from the many people in pathology offices that collect and ship blood samples for us.

Sincerely,
Georgia Chenevix-Trench
Chair, kConFab Executive Committee

The feedback from our readers is always so positive that we think the modest cost involved in producing the newsletter more frequently is well justified. However, we are interested in your comments, so if you think two newsletters a year is excessive, please let us know!

Left to right: Doone Lamb, Philippa McLean and Jennie Welzler at the Hallmark and National Breast Cancer Foundation launch "Card for a Cure" campaign, May 2004.

DUCTAL LAVAGE STUDY

Dr Gillian Mitchell, Medical Oncologist, and Mary Anne Young, Genetic Counsellor, Family Cancer Clinic, Peter MacCallum Cancer Centre, Melbourne.

A new research study is underway at the Peter MacCallum Cancer Centre and Royal Melbourne Hospital and we hope that it will be opening shortly at Westmead Hospital in Sydney. The study is investigating the role of the technique known as breast ductal lavage in the management of women at a high risk of developing breast cancer. The aim is to recruit 50 women, aged 25-65 years, who carry a BRCA1 or BRCA2 gene mutation. Recruitment may be opened later in the year to include women who have not had an informative gene test, but who have a strong family history of breast cancer.

Ductal lavage is a process where some of the cells lining the breast milk ducts are collected, using a plastic catheter, through the natural openings on the nipple surface. Breast cancer develops in the cells lining the milk ducts. If a woman not already at high risk for breast cancer is found to have abnormal ductal cells, her risk of developing breast cancer over the next 10 years increases. However, it is unknown whether the same is true for women already considered at high risk for breast cancer. We hope to answer this question through this study.

The plastic catheters used in the study are about the diameter of two human hairs. They are inserted into the nipple after the surface has been treated with an anaesthetic cream. To collect samples of the ductal cells, the duct is “lavaged” or “washed out” using a sterile saline solution. The cells are then analysed and if abnormal ductal cells are detected, then investigations are undertaken to locate any sign of breast cancer. If a cancer is detected, standard treatment is recommended. If no cancer is detected, more intensive breast surveillance will be offered for the next few years.

Several samples will be collected over a period of time to determine if analysis of these cells can help predict which women will go on to develop breast cancer. This could be very useful information for women deciding how best to manage their breast cancer risk, particularly those considering prophylactic mastectomy (breast removal). It may also help detect breast cancers not visible on mammograms. It is important, however, to emphasise that this technique will not replace mammograms or clinical breast examinations.

If you would like to find out more about this study, please contact Dr Gillian Mitchell at the Peter MacCallum Cancer Centre (03 9656 1199), Associate Professor Geoff Lindeman at the Royal Melbourne Hospital (03 9342 7151) or Associate Professor Judy Kirk at Westmead Hospital Sydney (02 9845 6947). More information about ductal lavage can also be found at the following websites: www.susanlovemd.com and www.ductallavage.com.

This is an extremely well tolerated procedure and is judged to be a similar level of discomfort or less uncomfortable than a mammogram by the majority of women who have had ductal lavage.

ATM – THE JURY IS OUT ON ITS ROLE IN HEREDITARY BREAST CANCER

There are currently two major breast/ovarian cancer susceptibility genes, known as BRCA1 and BRCA2. It is believed that other, as yet unidentified genes ('BRCAx') will explain some of the cancers that run in kConFab families. Recently, research by kConFab collaborators found alterations in a gene known as ATM that might predispose to breast cancer. ATM's normal job is to help repair damaged DNA- a routine but important task for virtually every cell in our body. DNA damage is a normal part of day-to-day existence, and repair is necessary to protect normal cells from accumulating genetic mistakes that could eventually lead to cancer. In fact, DNA repair is also one of the key functions of BRCA1 and BRCA2.

kConFab has studied several specific ATM alterations in families where no BRCA1 or BRCA2 mutation has been found. Two of these are of particular interest and have the somewhat cumbersome names '7271T>G' and 'IVS10-6T>G'. A small number of families were found to carry the alteration, which appeared to correlate with breast cancer risk within those families. This suggested that ATM could play a role in hereditary breast cancer. Indeed, it has long been believed by some that ATM may play a role in 'sporadic' (non-hereditary) breast and perhaps other cancers. In fact experiments using mice now support this idea.

One key question is whether these ATM findings can be used as a new genetic test (in addition to testing of BRCA1 and BRCA2) for high-risk individuals who attend Familial Cancer Centres. Unfortunately it now seems that the '7271T>G' alteration is extremely rare. No further Australian families have been identified, so it has not been possible to confirm whether it increases breast cancer risk. A role for 'IVS10-6T>G' was recently explored in a study by investigators at The Royal Melbourne Hospital, Genetic Health Services Victoria, SA Familial Cancer Service, and Westmead Hospital, Sydney. The findings suggest that the 'IVS10-6T>G' ATM alteration is not of use as a new genetic test. Indeed, it has now been found in Australians without a family history of breast cancer or any other disease for that matter.

Nevertheless, it is still possible that this alteration could in some way modify a woman's risk of developing breast cancer, in combination with other genetic factor(s). This question forms the basis of ongoing studies by kConFab on this important gene. A comprehensive analysis of the remainder of the ATM gene is also underway to determine whether there might be changes in other parts of ATM that could account for increased breast cancer susceptibility amongst women with a family history.

So the jury is still out on ATM.

Assoc Professor Geoff Lindeman
Head, Royal Melbourne Hospital Familial Cancer Centre and Co-Head, Victorian Breast Cancer Research Consortium Laboratory, Walter Eliza Hall Institute, Melbourne.

kConFab PSYCHOSOCIAL STUDY

The most exciting news with respect to the Psychosocial Study is that already some 1300 kConFab women are participating!! And in 2004, we will start to do the first follow-up interviews and questionnaires three years after recruitment. So, those of you who participated in the Psychosocial Study in 2001 will be hearing from us again in 2004. For those who have not yet heard from us, we are continuing to recruit both new and existing kConFab women who do not have cancer. We are aiming to recruit at least 2000 women.

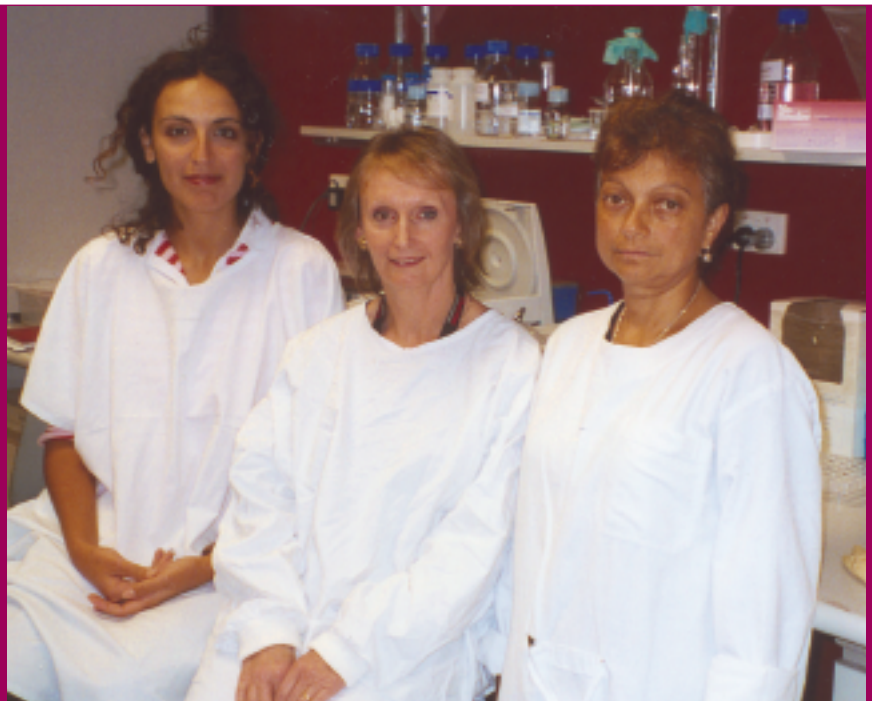
The Psychosocial Study is examining the role of life event stress, social support and other common psychological states such as anxiety and depression in the development of breast cancer. The study is being conducted from the Department of Psychological Medicine at the Royal North Shore Hospital, Sydney. Recruitment began in mid 2001, in conjunction with the Psycho-Immunology Study (now completed) and the Clinical Follow-up Studies. The National Health and Medical Research Council of Australia is funding this study.

This research has grown from a common belief that stress and other psychosocial factors may affect the risk of developing cancer, in particular breast cancer. It is unclear from existing research whether psychosocial factors such as stress can and do clinically alter cancer risk; and if so over what sort of time frame. The Psychosocial Study provides a unique and important opportunity for us to understand more about how these factors may influence the risk of developing cancer and how psychosocial risk factors may interact with familial and other risk factors. In addition, this study provides the potential for identifying specific risk factors that may be modified to reduce individual cancer risk.

Participation involves completing a questionnaire about emotional responses, thoughts and feelings, and social support. We also request a telephone interview in which we ask about recent situations of stress or change (this usually takes about 45 minutes). Sometimes these situations are related to cancer, but just as often we hear about various sources of stress, related to relationships, other health issues, work, finances, and other aspects of life. We are planning to interview participants every 3 years, to make sure we are up-to-date with what is going on in people's lives.

Our team works flexible hours, enabling telephone interviews to be conducted on days, evenings and weekends, around participant's family and work commitments, and even if you are living overseas. If you have any questions or require assistance with any part of this study, please call our toll free numbers at Royal North Shore Hospital on 1800 772 838 (Australia) or 0800 888 340 (New Zealand).

Dr Melanie Price
Psychosocial Study Coordinator
1800 772 838 (Australia)
0800 888 340 (New Zealand)



kConFab labaratory staff Danni Surace, Jan Groves and Lynda Williams.

THE PSYCHOLOGICAL IMPACT OF GENETIC TESTING FOR BREAST CANCER GENES – RESEARCH UPDATE FROM WA

By Professor Christobel Saunders, Breast Surgeon, QE11 Medical Centre, Perth

Breast cancer remains one of the most common forms of cancer in Australia. The average woman has a 1 in 12 chance of developing the disease. Women with a strong family history have an even greater risk of developing breast cancer. In 1994 and 1995, scientists discovered two genes with a strong correlation to breast and ovarian cancer. Mutations in the BRCA1 and BRCA2 genes are thought to be responsible for 5% of all breast cancers and more significantly, approximately one-third of familial breast cancers. Current evidence suggests that women who carry known BRCA mutations have a lifetime risk of developing breast cancer of above 50%.

In Western Australia, women who are at a high risk of developing familial breast cancer are provided with a modified management plan that includes increased screening and surveillance practices. This includes genetic testing for the BRCA1 and BRCA2 genes when possible. Unfortunately only certain mutations in these two genes can be identified by geneticists. Consequently the results of genetic testing can be either 'positive' or 'no known mutation'.

The psychological implications of genetic testing are obvious and because of this all high risk women participate in genetic counselling before any testing is conducted. In general however, the results of genetic testing have no impact on the nature of the counselling received.

In 2003 an audit was done to determine whether the psychological impact of genetic testing varied based upon the results received. This looked at three groups of patients attending the Royal Perth Hospital High Risk/Familial Clinic. These women were either found to have a mutation in one of the BRCA genes, had no known mutation or were untested for a genetic mutation but at high risk based on their family history.

We found over half of our patients were anxious due to their high risk status. The highest level of anxiety was seen in women with no known mutation while those who were BRCA positive were the least anxious. Women who had no known mutation also reported the highest level of concern with regard to passing on defective genes to their offspring and had most changed their outlook on life due to their genetic test results. Again the lowest level of concern and change in life outlook was found in those who were BRCA positive.

The reasons why this is the case is still unclear. It can be argued that women with a known BRCA mutation would have higher levels of emotional stability because they are aware of their BRCA status and the implications this will have on their disease process. Conversely a significant degree of uncertainty surrounds an inconclusive genetic test result (no known mutation), which may manifest as higher levels of distress and anxiety.

So what does this all mean for women undergoing genetic testing for the BRCA genes?

This audit, along with other work in the literature, suggests a need for individually tailored genetic counselling both before and after genetic testing as well as better use of the support services present in Western Australia. However it may also give some comfort to women considering undergoing gene testing: that knowledge of a positive result may bring more peace of mind than the uncertainty of not having been tested. If you are considering genetic testing or have already received test results, we encourage you to maintain effective and open communication with your family, friends and health care professional. Numerous support services exist which focus on both breast cancer and cancer in general. Information on these services can be obtained from organisations like BreastScreen WA and the Cancer Council of WA. Through communication and the utilisation of such services, it is hoped that the psychological impact of genetic testing for breast cancer can be minimised.

Any questions or comments can be directed to Professor Christobel Saunders (saunderc@cyllene.uwa.edu.au)

Please note: Information, services and advice can be obtained from any of the Family Cancer Clinics located in all States. Contact details for the Family Cancer Clinics can be found on the back page of this newsletter.

WHO WAS KATHLEEN CUNINGHAM?

Dr Kathleen Cuningham was a pioneer of breast cancer treatment in Australia, with a career spanning over 43 years.

Born on 2nd November 1898, and educated at PLC Croydon and the University of Sydney, Dr Cuningham graduated as a Bachelor of Medicine in 1921, and in 1927 joined the Rachel Forster Hospital for Women and Children. In 1939 she gained the Degree of Master of Surgery at the University of Sydney, an unusual accomplishment for a woman of her day, particularly one who carried on a busy general practice as well as honorary hospital duties. In 1941 she was elected as a Fellow of the Royal Australasian College of Surgeons (FRACS), the seventh woman to be admitted and only the second to be admitted in general surgery. A breast cancer research support organization, the Kathleen Cuningham Foundation (KCF), was named after this important medical figure, and the KCF provided the funding to start this research study, which we called kConFab (the Kathleen Cuningham Consortium for research on Familial breast cancer). The Kathleen Cuningham Foundation has since become known as the National Breast Cancer Foundation (NBCF), and we continue to value their on-going support for this project.

NEWS BREAKS

The Hereditary Cancer Clinic at the Prince of Wales Hospital, Sydney is pleased to announce a new Associate Genetic Counsellor Angela Overkov and welcome her on board. Angela can be contacted on 02 9382 2577.

A new study that involves partners is also underway and has been well received by families involved with the clinic. This study is being conducted at the site and is looking at the impact of one's partner being at risk of breast cancer. We may be underestimating the impact in some families but most spouses cope remarkably well. There is conflict between the need to be supportive, bear the burden of decisions and allowing your spouse to make her own decisions. The research team will provide more results related to this study in future newsletters.
Dr Kathy Tucker, Clinical Geneticist, Head of Department.

The Breast Cancer Network Australia has a new resource. The 'MY JOURNEY' kit is a comprehensive information resource developed by women who have had breast cancer. It is available free of charge for those newly diagnosed with breast cancer. Please ring 1300 785 562 to obtain a kit.

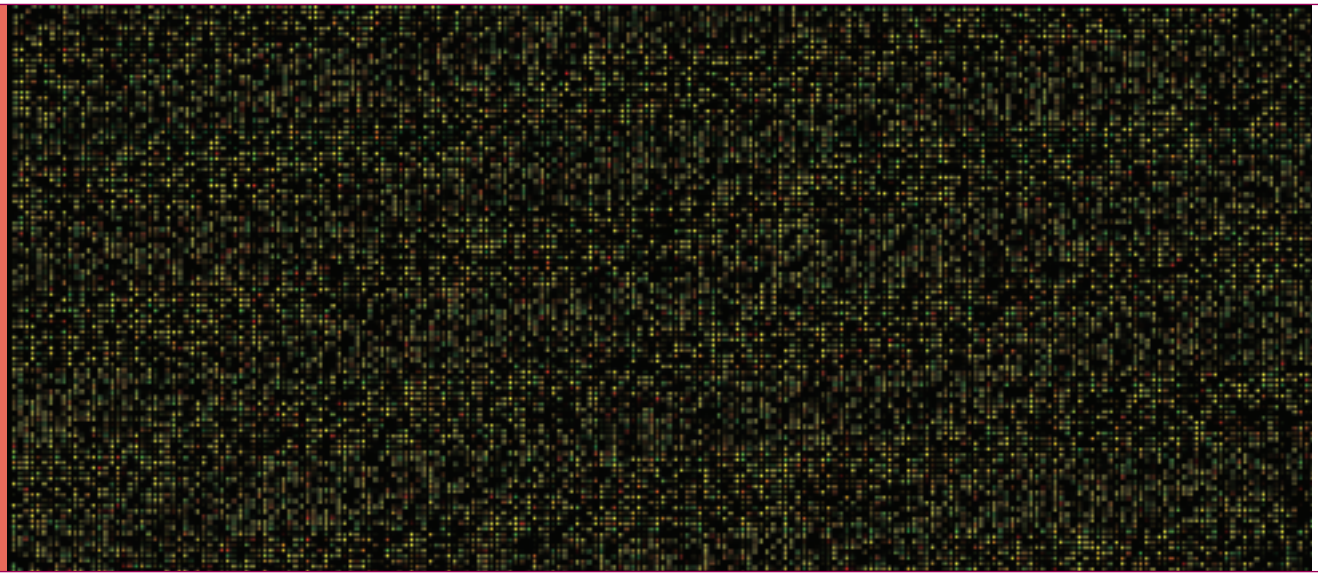
The National Breast Cancer Foundation will celebrate its 10th anniversary in October this year. Over this period research has made a significant contribution to the diagnosis, treatment and support of women with breast cancer and the Foundation has made a major contribution towards funding this progress. Check out the calendar of events and decide how you can join in to raise the power of 10 and help make breast cancer a thing of the past. For details call the Foundation on 02 9235 3444 or visit the web site www.nbcf.org.au

MEETINGS

Familial Cancer 2004: Research and Practice. The Family Cancer Clinics of Australia and New Zealand, kConFab and the Australian Ovarian Cancer Study (AOCS) annual meeting. Couran Cove 18th 22nd August 2004. Conference details and registration form can be found at http://www.kconfab.org

Still making a difference. Australia's 2nd National Breast Cancer Conference for Women organised by the Breast Cancer Network Australia. 27–29 August 2004. Melbourne Convention Centre, Melbourne. Please see website for information and registration. www.bcna.org.au or ring toll free 1800 500 258 for details.

The Victorian Breast Cancer Research Consortium in conjunction with the National Breast Cancer Foundation presents the Australian Breast Cancer Conference – research status, directions and priorities. Bio21Institute, Melbourne 17th – 18th November 2004 with a Public Lecture on 16 November, 2004 (venue to be announced). Details at www.vbcrc.org.au or contact VBCRC Executive Officer Clare Riglar at Clare.Riglar@cancervic.org.au or by phone on (03) 9635 5277.



MESSAGES FROM THE kConFab TEAM

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

- Because information is provided to our participants 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 family. In this case, we write notification letters to all participants who indicated a wish to be informed about results of genetic testing for the family. We do not supply individual research results, as our research testing is often done under conditions less stringent than those needed for a clinical test. 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 are interested in having 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 further contact with our study.

- Please tell your research nurse if you change your address.

COLLABORATING FAMILY CANCER CLINICS

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: Kate Pope
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: Kate Pope
Phone: 03 9342 4257

Victorian Clinical Genetics Service
Monash Medical Centre
Clayton
Contact: Ms Tarli Hall
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 to be appointed
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 Mike Gattas
Phone: 07 3253 1686
kConFab research nurse: Vicki Fennelly
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 7011
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 1725

Tasmania
The Royal Hobart Hospital
The Launceston 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: Kate Pope
Phone: 03 9342 4257

Auckland – New Zealand
Northern Regional Genetics Services
Auckland Hospital
Auckland, New Zealand
Contact: Dr Ingrid Winship
Phone: 64 9 3737599 ext 3768
kConFab research nurse: Jane Wylie
Phone International: 64 9 307 7232
NZ local call: 0800 476 123

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: 64 9 307 7232
NZ local call: 0800 476 123

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

USEFUL WWW SITES

Centre for Medical Consumers in NY – www.medicalconsumers.org
National Breast Cancer Foundation – www.nbcf.org.au
Breast Cancer Network Australia – www.bcna.org.au
Breast Cancer Research Association Inc – www.breastcancerasn.au