

kConFab

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Published by kConFab, Peter MacCallum Cancer Centre, St Andrew's Place East Melbourne, Vic 3002 Tel: (03) 9656 1542 Website: <http://www.kconfab.org>

DEAR READERS

Ten years have passed since kConFab held its first national scientific and clinical meeting, in combination with the Family Cancer Clinics in Australia and New Zealand.

This past week, while thinking about our progress over the past 10 years I pulled from the bookshelf a copy of our first conference book from 1998. Back then we held a one-day meeting with just 15 scientific and clinical talks, which covered all of the scientific and clinical research that was underway at that time on families at high risk of cancer. Our national meeting now runs over four full days and is attended by well over 300 clinicians, genetic counsellors and scientists. This year we expect that there will be over 60 formal oral talks and an equal number of poster presentations. Your involvement in kConFab by the donation of biological samples and clinical information has been the major driver of the large increase in breast, ovarian and prostate cancer research both in Australia and internationally. In this issue of the newsletter we have included updates about just eight of the many research projects that rely on the samples and data that you have so generously provided. We also currently have another 31 projects underway, each of which will add to our understanding of why so many cancers occur in your families and why these tumours often appear at an early age. The results of research projects over the last 10 years have led to great advances in our understanding of the genetic causes of breast, ovarian and prostate cancer. In turn, these advances have led to improved surveillance and clinical management of families at high genetic risk. We hope that the next 10 years will bring even more benefits.

An exciting advance is a recently-invented technology that will assist us to explore new ways to find genes involved in familial breast and ovarian cancer. A few years ago, the DNA sequences of the entire genomes of two humans were worked out, to great acclaim from the scientific community. Since then, the DNA sequences of three more people have been published. These achievements mark a tremendous stride forward in our ability to understand the genetic basis of diseases like breast cancer. The technology of DNA sequencing is advancing rapidly and its cost is decreasing rapidly. It should soon be possible to sequence a person's entire genome for a couple of thousand dollars. Within the next five years, the genomes of many individuals will be sequenced for research purposes and eventually as part of routine clinical care. Sequencing the genomes of kConFab families has not yet begun. But we have recently received requests from two groups of researchers who want to use a modified form of genomic sequencing to search for mutations that cause breast cancer in kConFab families.

Of course, the advent of genome sequencing raises a number of ethical issues. For example, who owns the DNA sequence? Who should have access to it and under what conditions? If genomic sequencing in research studies unexpectedly reveals that a person carries a mutation that may cause severe medical problems in the future, how should this information be best provided to the donor of the DNA? What obligations, if any, are owed to participants' blood relatives? None of these issues is new, but they have increased in significance now that genomic research sequencing is an immediate prospect.

For many years, kConFab has had an ethics

reference group that provides ethical advice and guidance to genetic researchers wishing to access the data and specimens donated to kConFab. Our ethics reference group, after carefully considering the risks and benefits of whole genome sequencing, believes that the knowledge gained from the technique has the potential to greatly advance our understanding of familial breast cancer. While acknowledging the ethical issues, the group considers that the best available technologies should be applied to familial cancer research, providing the work is scientifically valid. The group therefore recommended that kConFab material and data should be made available to researchers for genomic sequencing under the same strict conditions that are outlined in the ethical consent forms signed by all participants in kConFab. The next step is for kConFab to seek approval to go ahead with genomic sequencing from the Human Research Ethics Committees of the relevant hospitals and research institutes involved in kConFab research. We will keep you informed of progress. In the meantime, if you have concerns/questions about this issue, please do not hesitate to contact kConFab on the toll free number 1800 221 894.

Once again, thank you for your cooperation and willingness to participate in kConFab. Your involvement has been essential to the many advances in management, surveillance and clinical options now available through the Family Cancer Clinics and for placing Australian scientists and clinicians as leaders in this research.

Yours sincerely
Professor Joe Sambrook
Ph.D., FAA, FRS



PERSONAL STORIES

Sharon Tregoning – kConFab participant

My story is not unusual for kConFab newsletter readers. My sister Bess was advised of a diagnosis of breast cancer in January 2003. Our Dad had passed from bowel cancer in 2000. I had a benign lump removed in 1998, so I was concerned about the implications for me.

To try and resolve these concerns Bess & I went along to a familial cancer information meeting run by Peter MacCallum Familial Cancer Clinic. We wanted to find out if there was a link between breast and

bowel cancer. They advised that they were happy to investigate further if we could supply a detailed family history.

Bess got in touch with our aunt and a startling history revealed itself. 5 women in 4 successive generations had breast cancer and 3 of them were under 45 at diagnosis. This now made me at high risk. Bess underwent genetic testing, but no genetic mutation was able to be identified. Bess was thrilled; for me, I had no clear direction.

After undertaking a lot of research (and there was very little information available) and speaking with a few ladies who had undergone the procedure, I decided to have my breasts removed and re-built using tissue from my stomach.

So, in May last year, I underwent the surgery. I was on the operating table for approx 11 hours, in hospital for 10 days and took approx 3 months to be mostly recovered. I have since had my nipples reconstructed and tattooing

done to make them look more natural. My risk has gone from a possible 80% down to around 1%. The upside, apart of course from the main reason of reducing my cancer risk has been bigger breasts and a flat tummy!!

I have written a book on my journey which includes graphic photos of my recovery to assist other women facing the same situation to make an informed choice. It is called *Accepting With Grace – Mastectomy & Reconstruction, My Choice Before Breast Cancer*. My darling husband has also included a chapter that covers the experience from his experience and it is extremely moving.

The other significant result of my experience is the creation of breastANGELS – a not for profit I have founded that will fund breast reconstruction surgery for both women who have had breast cancer and also those at high risk.

To purchase, simply click here: www.breastANGELS.org/html/accepting.html



Krystal Barter

Krystal Barter was the first woman to beat the cancer that occurred in 5 generations of her family. Krystal, her grandmother and mother all carry a fault in the BRCA1 gene. The women in Krystal's family have faced breast cancer each at an increasingly earlier age - the youngest being her mum Julie at 36. Krystal remembers how her own level of anxiety increased when her mum was diagnosed.

Krystal decided to have a preventive mastectomy at age 25. A decision which she said was made easier, when she looked at her husband and two young boys both under 4 years old. "It was as much an emotional decision for me, as it was a physical one. I needed to be healthy for my boys."

Then the unthinkable happened at her last high risk screening. Her doctors had found changes in her breast which were indicative of early breast cancer. Krystal, unwilling to take the risk asked the doctors to move her mastectomy forward.

So on November 22nd 2008, Krystal Barter became the first woman in her family to change her destiny. After her prophylactic mastectomy, doctors told her the breast lump was hyperplasia (changing cells). If left untreated, it was only a matter of time before she too would join the list of women in her family affected by breast cancer.

For a long time Krystal struggled with the fact she felt alone. Even though she has such a supportive family she wanted that connection with other young women who were experiencing similar situations. Krystal decided that the best way to make the connection was through a web-site, **Pink Hope**, which was created by Krystal specifically for young individuals who are

affected or at a high risk of breast and ovarian cancer. The aim of the website is to inform, empower, inspire and support.

Pink Hope is under the umbrella of the National Breast Cancer Foundation and is endorsed by National Breast Ovarian Cancer Centre and kConFab. All money raised through Pink Hope goes directly to researchers in the form of a "**Pink Hope Grant**". Krystal believes the greatest gift we have in life is hope. Her family's struggle against breast and ovarian cancer has made her more determined to make a difference. "I don't want another young woman out there to feel the way I did, I want them to know Pink Hope is there for them and they are not alone".

Sign up and stay in touch with **Pink Hope** at www.pinkhope.org.au. Share your story or inspire other members on the Pink Hope forum and you could be selected as our "member of the month" which will win you a beautiful PANDORA gift valued at over \$200.

PALB2 - another BRCA2?

Mutations (faults) in a gene called PALB2 increase the chances of developing breast cancer and can be inherited (passed from one generation to the next) just like mutations in BRCA1 and BRCA2. Interestingly, the proteins made by the genes PALB2, BRCA2 and BRCA1 all work together to maintain healthy cells.

Mutations in PALB2 are not common (about 2% of families with several cases of breast cancer might carry such a mutation) but it could be very important to identify women with a

mutation in this gene because their chances of developing breast cancer could be very high, perhaps as high as the risks associated with having a mutation in the BRCA2 gene.

My laboratory is conducting a very large study involving more than 7,000 research participants (about 400 from kConFab) to try to find the best way to identify the women who carry a mutation in this gene and to find out more about their cancer risks. Our study has already identified several families who have a mutation in this gene and the data from these Australian

A/Prof Melissa Southey, Department of Pathology, The University of Melbourne

families are consistent with carriers having a substantial breast cancer risk. We have also formed an international group of breast cancer researchers from Australia, America, Canada, The United Kingdom and Finland who are interested in finding out more about PALB2 and clarifying its role in breast and other cancers. In the future, our work will help determine how a woman who carries a mutation in PALB2 might lower her risk of breast cancer, and should she become affected, how best to treat and manage her disease.

Help us make an IMPACT!

Research Updates

By now you have probably heard of the IMPACT study and may already be taking part. We currently have 167 men enrolled, with the overall aim to recruit approximately 250 men.

The study has been running for three years now and has opened in Victoria, South Australia, New South Wales and Western Australia. We are also very excited to be opening in Queensland and Tasmania later this year.

Thank you to everyone who is already participating in the study. We have had an enormous response and have in fact recruited a third of all men worldwide.

Later this year we will be writing to all the remaining 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

An update on the IMPACT study - (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 & Dr. Geoff Lindeman Royal Melbourne Hospital, Melbourne.

email familial.cancer@petermac.org to register your interest at any time.

What is the study?

This is an international study that was set up because men who are from families where there is an alteration (mutation) in the BRCA1 or BRCA2 genes 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 is 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 these questions, 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. This study will also help to work out more accurately the level of prostate cancer risks linked to these gene alterations.

Am I eligible to take part?

To be eligible for the study you need to be:

- Male
- Aged 40 to 69 years
- Part of a family where there is a BRCA1 or BRCA2 mutation present (It is not necessary for you to know this mutation test result to take part).
- Unaffected with prostate cancer

What does it involve?

The study involves a visit to a study hospital once a year for five years. At the visit you will be asked 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, you will be referred to a local urologist for further investigation which is likely to include a prostate biopsy done by the urologist. Any subsequent treatment will depend on the results of the PSA test and any prostate biopsy taken.

Examining the impact of a BRCA 1 or BRCA2 gene mutation on the development of prostate cancer

Dr Ivan MY Hoh and Associate Professor Damien Bolton, Urologists, Austin Health, Melbourne

The controversy on prostate cancer screening has never been more debated than now, due to two recently published US and European trials in The New England Journal of Medicine on the use of PSA blood test in preventing deaths due to prostate cancer.

After looking at a combined total of 250,000 men over 11 years of follow-up, the results suggest that by treating men with prostate cancer it may expose them to more risks than otherwise. The most startling find from the European trial, concluded that, in order to prevent one prostate cancer death, 1400 men had to be screened and only 50 men needed to be treated. This is potentially good news for men who were diagnosed with prostate cancer with the knowledge that they have a 1 in 50 chance of dying from prostate cancer

if left untreated. However, like any cancers, there exists a spectrum of "threat" arising from indolent or inactive through to aggressive ones, and we must be able to detect those aggressive ones in order to treat them. As yet, such method(s) do not exist, but there is some evidence that the answer lies for some men in the genetic make-up of the individual and more pertinently, in the breast cancer predisposition genes BRCA1 or BRCA2 gene. Previous kConFab research has demonstrated that the risk of developing prostate cancer can be as high as 4.7 times compared to the general population if the BRCA2 mutation is present. Significantly, these men tend to be younger and the prostate cancers were highly aggressive. Our recent pilot data have demonstrated that the youngest affected man with BRCA2 gene mutation was 43 years old and the mean duration to death from diagnosis was 4 years.

For this reason, kConFab, together with a multidisciplinary team from the University of Melbourne, Austin Health and the Peter Mac Cancer Centre Melbourne have come together to examine further this link between a BRCA gene mutation and prostate cancer. Whether this will herald new answers which in turn will lead to finding a cure for prostate cancer is too premature to conclude, but it is certainly a step in the right direction in our fight against prostate cancer. So far, we have received information from 180 kConFab men, so thank you to all of the men who have answered our questions and to the Australian and New Zealand urologists who aren't used to working with a breast cancer research group but who have all provided great help and assistance to us with data acquisition. If there has been a diagnosis of prostate cancer in your family that we haven't been updated about, please let us know by ringing 1800 221 894.

kConFab Clinical Follow-Up project

Associate Professor Kelly-Anne Phillips

Peter MacCallum Cancer Centre, Melbourne

We would like to extend our sincere thanks to all kConFab participants who have completed their Follow-Up questionnaires and helped make this project so successful.

What Do We Do?

The kConFab Follow-Up Project, initiated in 2001, mails questionnaires to kConFab participants every 3 years. Initially, questionnaires were sent to both men and women but due to funding constraints are now only sent to women. The questionnaire asks for updates on current health and lifestyle, and whether any new cancers have been found in the family. Our research assistants, Lucy Burnham and Kate Lucas, may contact participants to clarify information provided. An opt-out card is included or a message can be left on the toll free help line for those who are unable or do not want to complete the questionnaire. Participants will be contacted again in 3 years unless they request no further contact.

What Have We Learned?

Our project has produced several articles in international medical journals. The research has been presented at international meetings and has received three awards from the American Society of Clinical Oncology. The key messages from the research are:

Half of kConFab Participants Who Are At Average Risk for Breast Cancer Have Too Many Mammograms 1:

Some women in kConFab have been shown to be at average risk (rather than high risk) for breast cancer. We have shown that about 50% of such women undertake mammography too frequently or start too young according to National Health and Medical Research Council (NHMRC) guidelines. This can be harmful to their health. Women who are unsure of their level of breast cancer risk or the frequency of mammograms recommended for them personally are advised to contact their nearest Family Cancer Centre

Medication To Reduce The Risk Of Breast Cancer Is Available But Is Infrequently Used2:

The tablet medications, tamoxifen and raloxifene, reduce the risk of breast cancer by up to 50%. We have shown that only 1% of women in kConFab who are at high risk for breast cancer use these preventive treatments. This is much lower than in most

other countries. In a subsequent study of clinicians, which will be published in the next few months, we have shown that many do not discuss these medications with their patients. We are working to try and change this. Norman Swan examined this issue in a broadcast of the Health Report on Radio National 4/8/2008. www.abc.net.au/rn/healthreport/stories/2008/2320385.htm Those interested in learning more about the pros and cons of such medications can contact their nearest Family Cancer Centre.

Half the Women at High Risk for Breast Cancer Use Complementary and Alternative Medicines3:

Our surveys have shown that 48% of women at high risk for breast cancer use complementary and alternative medicines (CAM). These treatments are unproven so it is reassuring that only 11% do so specifically in the belief that it will reduce their risk of breast cancer. This research highlights the need for doctors to enquire about CAM use when taking a medical history from high risk women, given the potential for drug interactions.

For kConFab Women With Breast Cancer, The Likely Outcome of That Breast Cancer Does Not Seem To Influence Their Decision To Have Prophylactic Mastectomy On The Opposite Side:

About 15% of women in kConFab have their opposite healthy breast removed after their initial diagnosis of breast cancer. This decision to have their healthy breast removed does not seem to be influenced by the prognosis of their initial breast cancer or their mutation status. Younger women with breast cancer diagnosed in more recent years are the most likely to choose to have their opposite breast removed to prevent further cancer occurring. This research has received an award and will be presented at the forthcoming American Society of Clinical Oncology Meeting prior to publication in an international journal.

What Have We Got Planned?

Lumpectomy or Mastectomy for BRCA1 and BRCA2 Mutation Carriers - Which Is Better?

We have contributed information from the kConFab Follow-Up Project to a cooperative study with groups in the United States, Spain and Israel looking at the results of breast conservation surgery (lumpectomy) versus mastectomy for BRCA1/BRCA2 carriers. This work was led by Professor Lori Pierce at the University of Michigan. The resulting

publication is nearing completion and we hope to share the very interesting results with you in a future newsletter.

Role of Prevention Medications in BRCA1 and BRCA2 Carriers:

We are leading an international cooperative effort with groups from the United States, Canada and Europe to further examine the role of breast cancer prevention medications in women who carry mutations in BRCA1 or BRCA2.

How Do Psychological and Social Factors Influence the Screening Behaviours of High Risk Women?

We are currently working with the kConFab Psychosocial Study on a study which will address this question.

How Do Lifestyle Factors Affect the High Risk Woman's Risk of Breast Cancer?

There is some information already available about this, but much of it is of questionable quality. We are working with groups in the United States, Canada and Europe to answer this question in a high quality study, so that we give you the right answers.

Watch This Space

We are currently planning our own Webpage which will be accessed via a link from the main kConFab page. We anticipate this will be a great place for you to get regular updates on how you are helping us answer the questions that are of importance to women at high risk for breast cancer.

Ms Prue Weideman

**Clinical Follow-up Project Coordinator
Toll free telephone no:**

Australia 1800 111 581

New Zealand 0800 230 029

1. Dawson SJ, et al Cancer risk management practices of non-carriers within BRCA1/2 mutation positive families in the Kathleen Cunningham Consortium for Research into Familial Breast Cancer (kConFab). *Journal of Clinical Oncology* 2008; 26: 225-32
2. Phillips KA et al. Risk-Reducing Surgery, Screening and Chemoprevention Practices Of BRCA1 And BRCA2 Mutation Carriers: A Prospective Cohort Study. *Clinical Genetics* 2006; 70: 198-206
3. Field KM, et al. Predictors of the Use of Complementary and Alternative Medicine (CAM) By Women At High Risk For Breast Cancer. *European Journal of Cancer* 2009, 45:551-560

Magnetic Resonance Imaging (MRI) in women at high risk of breast cancer.

Professor Christobel Saunders & Toni Musiello, QE11 Medical Centre, Perth



Since February 2009, the Australian Government has provided Medicare rebates for annual breast Magnetic Resonance Imaging (MRI) scans of women less than 50 years of age, with no signs or symptoms of breast cancer, but who are at high risk of developing breast cancer.

In accordance with the National Breast and Ovarian Cancer Centre's (NBOCC) recommendations, women at high risk have been defined as having one of the following:

- (a) Three or more first or second degree relatives, on the same side of the family, who have been diagnosed with breast or ovarian cancer;
- (b) Two or more first or second degree relatives, on the same side of the family, who have been diagnosed with breast or ovarian cancer, which include one of the following features:
 - bilateral cancer;
 - onset of breast cancer before 40 years of age;
 - onset of ovarian cancer before 50 years of age;
 - breast and ovarian cancer in the one relative;
 - Ashkenazi Jewish ancestry; or
 - breast cancer in a male relative;
- (c) One first or second degree relative diagnosed with breast cancer at 45 years or younger, plus another first or second relative on the

same side of the family with bone or soft tissue sarcoma at age 45 years or younger;

(d) Genetic testing has identified the presence of a high risk breast cancer gene mutation.

In the last few years research studies have demonstrated the value of breast MRI as part of surveillance for women at high-risk. MR imaging of the breast is reported to have high sensitivity but lower specificity than mammography. This means that whilst MRI is better than mammography at identifying that cancer is present, MRI does "see" more lesions that turn out not to be cancer, and may need further investigation including a biopsy. This can be complex as lesions seen only on MRI can be difficult to localize for biopsy – this stresses the importance of having an MRI as part of an overall surveillance strategy that includes specialist clinical care and an expert team including those with special expertise in breast imaging including MRI.

Current surveillance recommendations for women at high risk include regular self examination, 6 monthly consultation examination by a health professional, and annual mammogram and breast MRI – all co-ordinated by a specialist high risk clinic.

Controversies include:

- Why only under 50 years?

This is where we have evidence of benefit from studies, and this is probably because many breast cancers in high risk women occur under 50, and over 50 most women's breasts are easier to "read" on the mammogram so detection of a cancer is easier.

- What age should the MRIs start?

Usually this is recommended around 35 or 40 years, but may depend on what age the earliest cancer in the family occurred.

- If a woman has had breast cancer can she still get the rebate for surveillance MRI?

It is our opinion from interpretation of the government guidelines that if a woman is at HIGH RISK on the above criteria but has no CURRENT breast symptoms, then the rebate is applicable whether she has had prior cancer or not.

- What if an abnormality is seen on the MRI?

The rebate does include a further MR test within the one year period if an abnormality is seen to allow it to be investigated or followed up.

For more information on the rebate visit:
<http://www.health.gov.au/internet/main/publishing.nsf/Content/mri-breast-qa>

kConFab Psychosocial Study

Dr Melanie Price, University of Sydney

The kConFab Psychosocial study has now been going for nine years, with the aim of examining whether psychosocial factors such as stress, depression, social support and personality play a role in increasing the risk of developing breast cancer. For this study, participants are contacted once every 3 years over a 10 year period and complete a questionnaire (in about 15 minutes) and a telephone interview (about 45 minutes) to tell us more about their recent stressful life events. Over 2300 women have completed the first interview and questionnaire, 1540 women have completed the second, and some 350 women have completed the third and final follow-up for this study, 6 years after they started the study.

While the main results of the Psychosocial Study are still some years away, results of several questions have been published in medical journals. Some of these have been written together with the Psychosocial Study and the Clinical Follow-Up Study. These include one on

mammography screening of non-carriers from BRCA mutation positive families, and the use of complementary and alternative (CAM) medicine.

One other question we have been looking at is how anxious (or worried) women were about being at increased risk of breast cancer, and what sort of factors influenced cancer worry. We found that, day to day, most women do not have high levels of cancer related worry, even though, on average they estimated their lifetime risk of developing breast cancer (perceived risk) was 50.3%. In fact, perceived risk was only one of the factors associated with cancer worry. Not surprisingly, there will be times when cancer related worry will be increased, such as a finding out that you personally carry the BRCA1 or BRCA2 mutation, or when a family member is diagnosed with cancer. We found that these types of experiences increased cancer related worry, over and above a woman's sense of her risk. Therefore, even if a woman is able to quote her risk of breast cancer quite accurately and understands that she is in no way certain of developing cancer, if she has had very difficult experiences in her

family with cancer, or is in general, a "worrier", then her breast cancer worry might be elevated. We also found that being closer in age to the age of the youngest family member who has been diagnosed with cancer, was associated with increased cancer worry, suggesting that people interpret their own place within the family history and possibly alter their perceptions of their immediate risk, and therefore worry, accordingly. As the gap between this first diagnosis and their own age widens, they feel less vulnerable.

Further results arising from the psychosocial study will be reported in this newsletter as they become available.

Thank you to all women who have taken the time and effort to complete the questionnaire and share with us their life events in the interview. The success of the Psychosocial Study depends on them and we appreciate their generosity.

Please do not hesitate to call our toll free numbers below if you have any questions or concerns about the study so far. Also, please could you update us on any change of address or contact information.

kConFab Psychosocial Study Team
Toll-free call Australia: 1800 772 838
Toll-free call New Zealand: 0800 888 340

Intimacy and closeness improves the experience of couples living with cancer.

A new University of Western Sydney research project will aim to make the experience of cancer more manageable by helping couples reclaim closeness and intimacy in their relationships. The project will be conducted in association with Westmead Hospital, Nepean Hospital, the National Breast Cancer Foundation, and the Cancer Council of New South Wales.

People with cancer, or people who have had cancer, and their intimate partners are invited to take part in the study, which aims to develop new programs that will help people communicate their sexual desires and needs with their partners and allow them to re-negotiate their sexual lives.

The study is also interested in talking to health professionals working in oncology. For more information, or to take part in the study, contact Caroline Joyce, Project Coordinator, toll free on 1800 19 20 02. You can also email her at cancerandsexuality@uws.edu.au or fill in the questionnaire on line at <http://www.uws.edu.au/cancerandsexuality>

Upcoming events:

Familial Cancer 2009: Research and Practice

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

Venue: Mantra on Salt Beach, Kingscliff, Queensland

Dates: 11th – 14th August 2009

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

The Friends of kConFab 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**.

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. 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.
- 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 all 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.

- **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.
- It has come to our attention that some participants may not have received the 2008 newsletter due to an error with the auto generated mailing list. We know that our newsletters are greatly appreciated due to the many research and clinical updates in each edition so we apologise for this error and have corrected the systems fault so this error will not occur again. Should you wish to view the 2008 newsletter or any other newsletter edition, please go to the kConFab home page at www.kconfab.org as all the editions are featured on the first page.

Speakers list – we are still looking for more people.

Thank you all of the kConFab members who contacted us after the last newsletter to place their name on our speakers list at kConFab, we work closely with breast cancer groups such as the National Breast Cancer Foundation by offering to talk about our research at their fundraising events.

We are also sometimes asked by these groups to nominate people from kConFab families who might wish to speak about their family experience at these functions. For this reason we have set up a kConFab speakers' registry. You don't have to be a professional

speaker to add your name to this list.

In fact, we find the best speakers are sometimes those with no professional speaking experience but able to speak from the heart about their families and how research can offer hope to future generations. Speakers are normally asked to only give a brief 10-minute presentation. If you wish to add your name to the registry, please call Heather on the kConFab toll free number 1800 221 894 or email heather.thorne@petermac.org. We would ideally like to have male and female representatives from all States.

Breast stem cells - trying to get abreast of breast cancer

Our group is trying to understand how breast stem cells or their descendants (called 'progenitor' cells) play a role in breast cancer. The breast stem cell is like a seed that gives rise to all the ducts and milk-producing cells in the breast. Stem cells are required for replenishing breast tissue during normal monthly cycles in women and for generating new breast tissue during pregnancy and lactation. It is possible that the stem cell, which is long-lived, may be an important 'target cell' in which genetic mishaps progressively accumulate, ultimately leading to breast cancer.

A few years ago our team discovered breast stem cells in mice. Remarkably, even a single stem cell was able to give rise to a complete functional mammary gland. The stem cell was found to resemble a subtype of breast cancer that commonly occurs in BRCA1 mutation carriers. This has fuelled speculation that a stem cell, or an early descendant cell, can give rise to BRCA1-associated breast cancers.

We have now turned our efforts to discovering stem and progenitor cells in human breast tissue. A priority is to understand whether stem or progenitor cells are directly linked to the development of BRCA1- and BRCA2-associated breast cancers. In the longer-term, we hope that this research

will pave the way for the identification of specific breast cancer markers. These could potentially be used in cancer diagnosis or even serve as new therapeutic targets for treating or preventing breast cancer.

Our group has obtained ethics approval to study fresh breast tissue from kConFab women undergoing prophylactic mastectomy or surgery for breast cancer. Normally the pathologist examines some of

the tissue for diagnostic purposes, and the remainder is simply discarded. By donating this unwanted tissue, kConFab women are helping to fuel our research efforts. Around the world there are very few groups like kConFab that are able to provide support for this kind of research. We hope that the generous participation of kConFab women, combined with our research efforts, will have a positive impact on future generations with a strong family history of cancer.



Associate Professor Jane Visvader, The Walter and Eliza Hall Institute and Associate Professor Geoff Lindeman, The Walter and Eliza Hall Institute and Royal Melbourne Hospital.

Low risk genes and high risk genes

*Associate Professor Georgia Chenevix Trench
QIMR, Royal Brisbane Hospital, Queensland*

During the last 10-20 years, researchers from all over the world have worked together to identify those individuals at greatest risk of developing life-threatening diseases. We now know that, in most cases, the risk of developing a disease is determined by a combination of genetic susceptibility ("nature") and environment ("nurture"). For some diseases – lung cancer, for example, a single environmental factor – smoking – is very strongly associated with risk. But in the case of breast and ovarian cancer, environmental or life-style risk factors turn out to be only weakly related to the risk of developing disease. Instead much of the risk of developing breast cancer seems to be genetic. In the

last decade, several genes e.g BRCA1 and BRCA2 have been identified that predispose strongly to breast cancer. However, only about 30% of kConFab families carry mutations in these genes. So what genes are responsible for breast cancer in the rest of the families?

Low risk genes

In the last two years, very rapid progress has been made by the international breast cancer research community in identifying additional genes that predispose to breast cancer. kConFab has played an important part in this work by participating in two huge international consortia, the Breast Cancer Association Consortium (BCAC) and the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). In total, ten new breast cancer predisposition genes have been identified by BCAC, and most of these have

also been shown by CIMBA to influence the age of onset of breast cancer in carriers of BRCA1 and BRCA2 mutations. However, the effect of each one of these newly-found genes on breast cancer risk is very small, and it is likely that many more such genes remain to be found. For this reason, these new genes are not being used clinically in Australia to predict a woman's breast cancer risk,

BCAC and CIMBA, along with consortia studying prostate and ovarian cancer, have recently received a large grant from the European Commission to continue their work. The main aims of the project will be to identify more breast cancer susceptibility genes, and to work out whether women who carry particular versions of these new 'low risk' genes are more liable to develop breast cancer if they are subjected to particular lifestyle or environmental risk factors.

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
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kConFab research nurse: Kate Mahendran
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: Belinda Zielony
Phone: 02 9382 2607

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

**St Vincent's Hospital
Family Cancer Clinic**
Darlinghurst, 2010
Contact: Dr Allan Spiegelman
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The John Hunter Hospital
Hunter Valley, NSW
Contact: Dr Allan Spiegelman
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kConFab research nurse: Belinda Zielony
Phone: 02 9382 2607

Brisbane

**Queensland Clinical Genetics Service
Royal Children's Hospital**
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Herston, 4029
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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
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Phone: 08 8161 6995
kConFab research nurse: To be appointed
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Perth

**Genetic Services of Western Australia
King Edward Memorial Hospital**
374 Bagot Road
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Tasmania

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The Launceston General Hospital
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Auckland – New Zealand

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Wellington – New Zealand

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