

The importance of biobanks in translational oncology

Amber Willems
kConFab
Melbourne, Australia

Kathleen
Cunningham
Foundation

kConFab

CONsortium for
research into
FAMILIAL Breast Cancer

www.kconfab.org

The importance of biobanks in translational oncology

kConFab

- a national multidisciplinary consortium of ~150 researchers
geneticists, oncologists, surgeons, genetic counsellors
psychologists, pathologists, epidemiologists
- focused on genetic epidemiology of familial breast/ovarian cancer
- collects comprehensive clinical, genetic, epidemiological data and biospecimens from multicase families in all States and Territories
- makes data and specimens available to researchers for use in peer-reviewed, ethically-approved and funded research projects

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- has developed best-practice protocols for collection of data and materials for research
- provides family cancer clinics with evidence-based guidelines for clinical activities (under a research umbrella)
- plays a pivotal role in multicentre, national and international research in genetic epidemiology and psychosocial care (22 sites within Aus/NZ & Clinical Follow-Up)
- fosters community involvement in research (annual newsletter)

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Progress to date

- Families completed 1284
- Average number of bloods/completed family 8.7
- Breast cancers 6685
- Epi questionnaires 11346
- Pathology reports 7669
- Fresh tissue specimens 703
- kConFab supports 80 research projects world-wide
- 71 papers published using kConFab materials/data

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Breast Cancer Res Treat
DOI 10.1007/s10549-008-0064-8

EPIDEMIOLOGY

LETTERS

Familial Cancer (2008) 7:151–155
DOI 10.1007/s10689-007-9162-8

Is *MSH2* a breast cancer susceptibility gene?

EE Ming Wong · Andrea A. Tesoriero · Gulieta M. Pupo · **kConFab** ·
ABCFS · Margaret R. E. McCredie · Graham G. Giles · John L. Hopper ·
Graham J. Mann · David E. Goldgar · Melissa C. Southey

Springer Publishing Group <http://www.nature.com/naturegenetics>

A common breast cancer

Angela Cox^{1,33}, Alison M
Karen A Pooley², Serena
Louise Brinton³, Beata P
Olivia Fletcher⁹, Nichola
Christen K Axelsson¹⁰, D
Silke Kropp¹³, Angela R
Rainer Fagerholm¹⁷, Kirs
Michael R Stratton¹⁹, Na
Amanda B Spurdle²², Ge
Familial Breast Cancer, J
Fergus J Couch²⁴, Janet
Laura J Van't Veer²⁵, Da
Per Hall²⁹, Yen-Ling Low
Alice J Sigurdson³², Den
Douglas F Easton², on b

Breast Cancer Res Treat
DOI 10.1007/s10549-008-0083-5

PRECLINICAL STUDY

No evidence that *CDKN1B* (p27) polymorphisms modify breast cancer risk in *BRCA1* and *BRCA2* mutation carriers

Amanda B. Spurdle · Andrew J. Deans · David Duffy · David E. Goldgar ·
Xiaoqing Chen · Jonathan Beesley · **kConFab** · Douglas F. Easton ·
Antonis C. Antoniou · Susan Peock · Margaret Cook · EMBRACE Study Collaborators ·
Katherine L. Nathanson · Susan M. Domchek · Grant A. MacArthur ·
Georgia Chenevix-Trench

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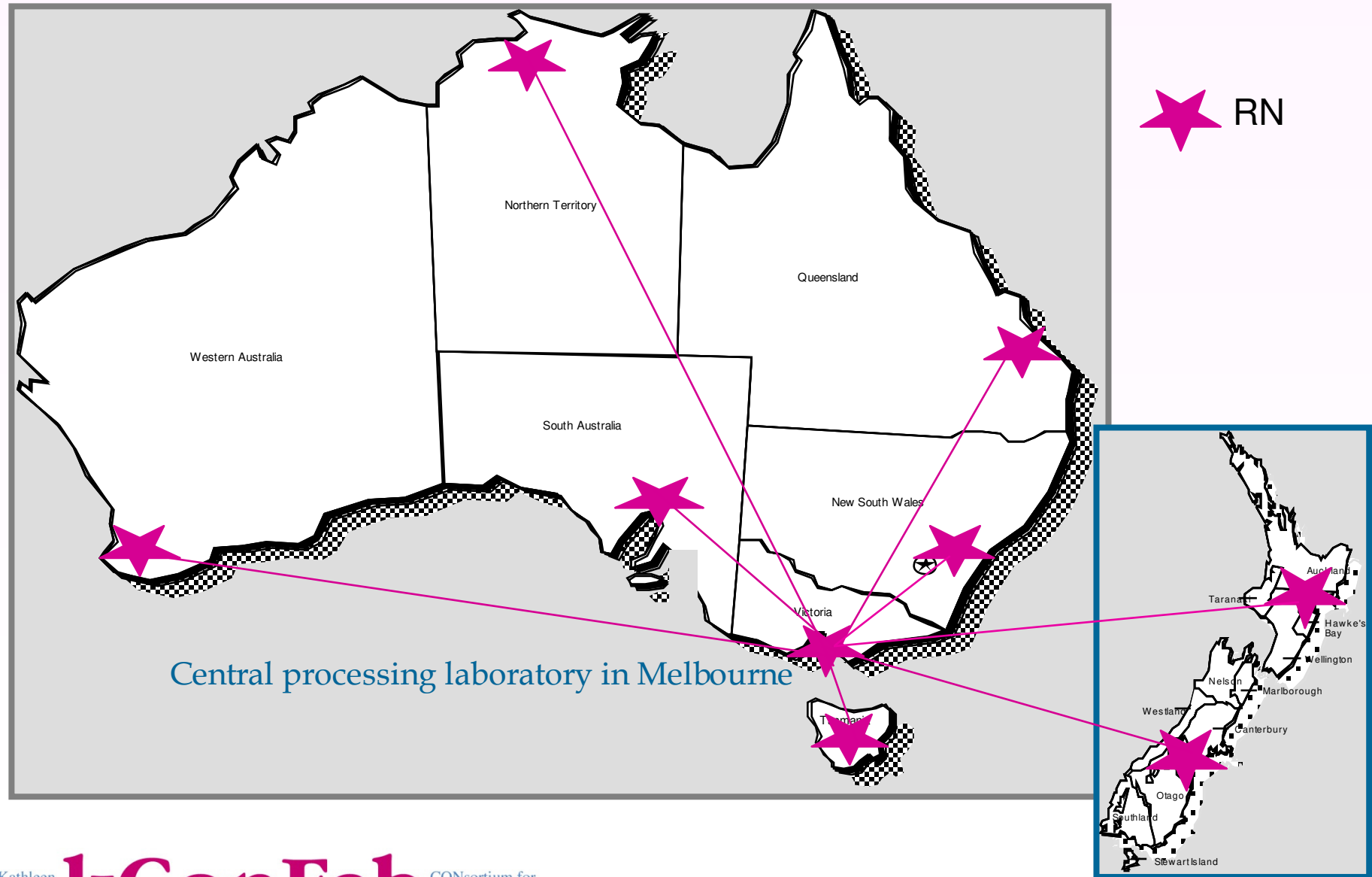
- **Biorepository**
 - Blood (plasma, wbc, nl, blood pellet)
 - Tissue (breast, ovarian, prostate)
 - Fresh - normal (prophylactic)
- tumour
 - Archival - slides (stained/unstained)
- paraffin block
 - Establish LCLs
 - 'unlimited' DNA
 - 'unlimited' RNA

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- **Knowledgebase** (~330 additional data fields)
 - patient information (e.g. gender; d.o.b; d.o.d; reproductive history)
 - genetic information (e.g. family mutation, gene, level of testing, mutation effect, haplotype)
 - epidemiological information (e.g. height/weight; education level; ethnicity & religion; lifestyle factors: smoking, alcohol, diet)
 - medical details (e.g. cancer site, type of tumour; date of cancer diagnosis, age at diagnosis; cancer pathology: morphology, topography, behaviour, grade, hormone receptor status; treatment/medical history; OCP or HRT history)

How does kConFab operate?

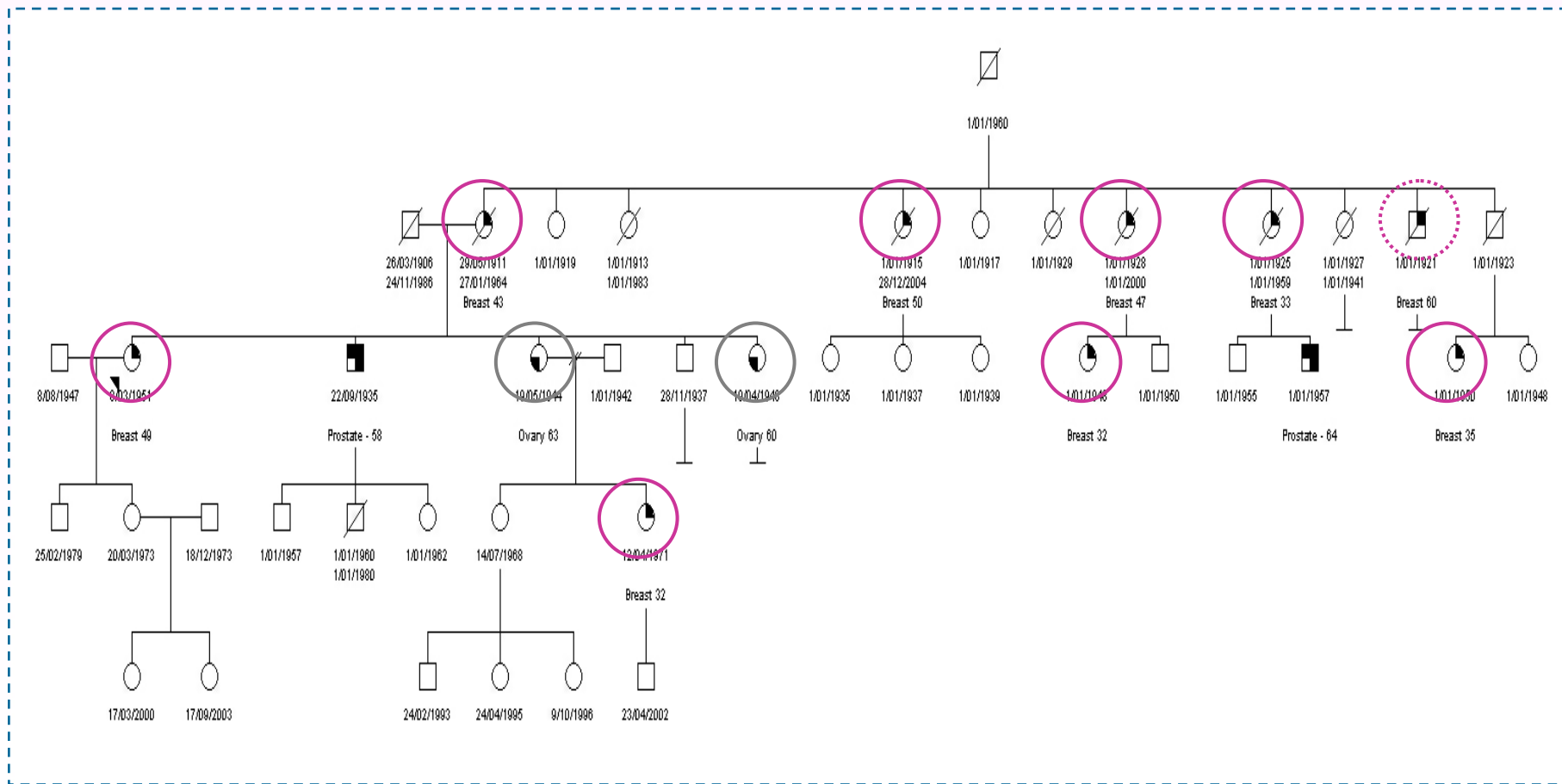


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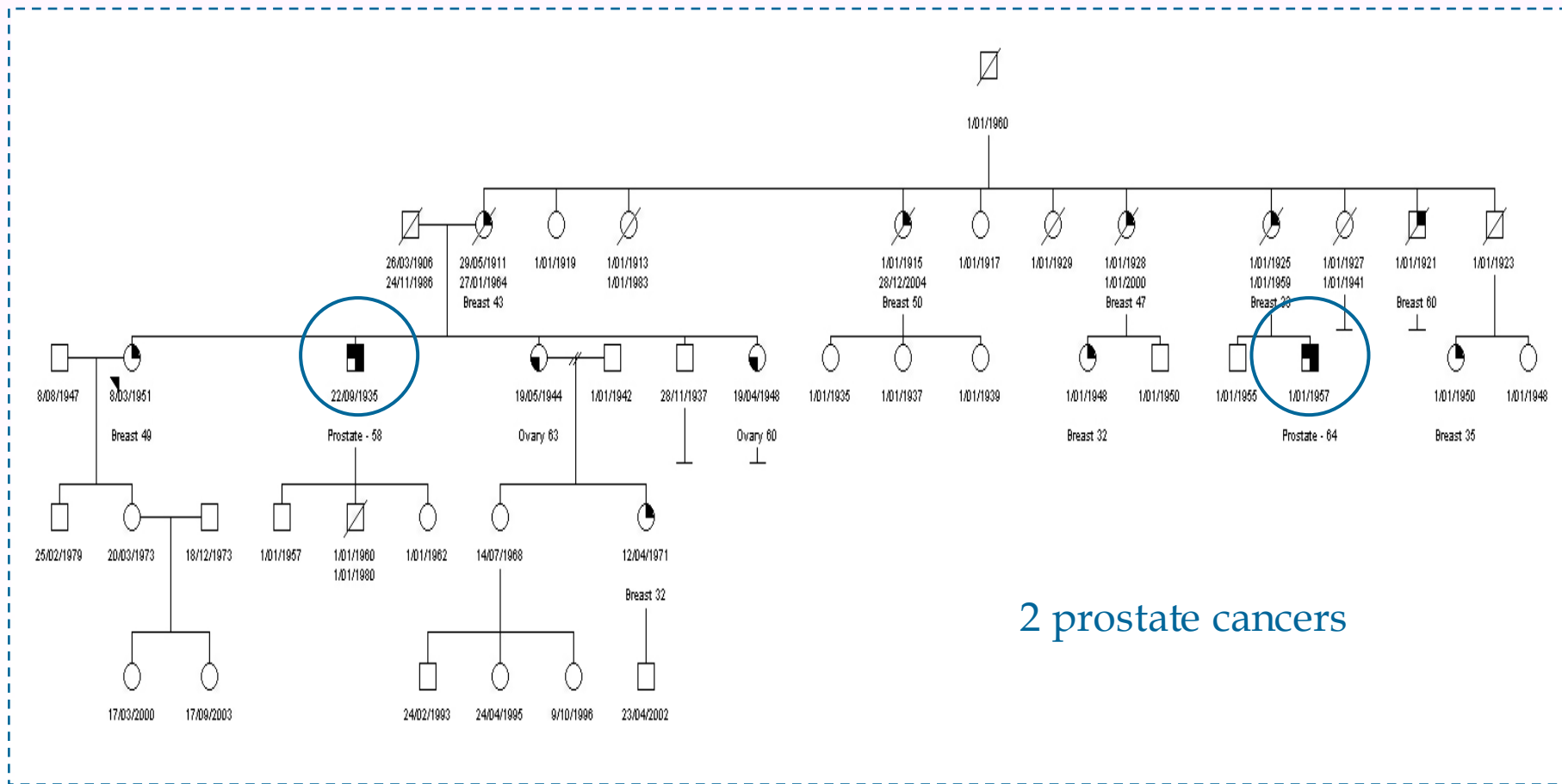
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9 diagnosed with breast cancer incl. 1 male breast cancer; plus 2 ovarian cancers.
All under the age of 45 years – 6 in their 30's

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In Total:
 Affected: 815
 Path Reports: 150

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What is the significance of **prostate** cancer in the kConFab breast cancer families?

- Is it expected? (prostate cancer is common - 1/11) within general population
- Does the genetic fault that causes breast cancer (*BRCA1* or *BRCA2*), also cause prostate cancer in these family members?

The association between a *BRCA1* or *BRCA2* mutation and prostate cancer through genetic analysis is of paramount importance in further understanding the risk of prostate cancer to men with these families.

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Aim:

To utilise the extensive resources available in the kConFab biospecimen bank to:

- 1) Examine if a causal relationship exists between pathogenic germline mutations in *BRCA1/2* and prostate cancer
- 2) Analyse clinical and histopathological features of prostate cancers in individuals who carry a pathogenic germline *BRCA1* or *BRCA2* mutation

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What was required from the kConFab biospecimen bank?

Access to:

- Archival prostate tissue specimens
 - Stained and unstained sections: DNA extraction from tumour cells for MLPA analysis and DNA sequencing
- Blood specimen (where applicable)
 - Confirmatory genetic testing of germline DNA
- Pathology review of prostate tumour specimens
 - Assessment of clinical and pathological features
- Medical information
 - Date of diagnosis, type of surgery, cause of death & date (if applicable), PSA level at diagnosis
- Genetic information
 - Mutation carriers (pathogenic germline) were required for the study

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DOI 10.1007/s10549-006-4

Familial Cancer (2008) 7:151–155

DOI 10.1007/s10689-007-9162-8

Human Cancer Biology

Loss of Heterozygosity at the *BRCA2* Locus Detected by Multiplex Ligation-Dependent Probe Amplification is Common in Prostate Cancers from Men with a Germline *BRCA2* Mutation

Amber J. Willems,¹ Sarah-Jane Dawson,² Hema Samaratunga,⁴ Alessandro De Luca,⁵ Yoland C. Antill,² John L. Hopper,³ Heather J. Thorne¹ and kConFab Investigators

Clinical Cancer Research (2008), **14**, p.2953-2961.

Amber J. Willems, Deborah J. Sigafoos, Douglas F. Easton², on b

Katherine L. Nathanson · Susan M. Domchek · Grant A. MacArthur · Georgia Chenevix-Trench

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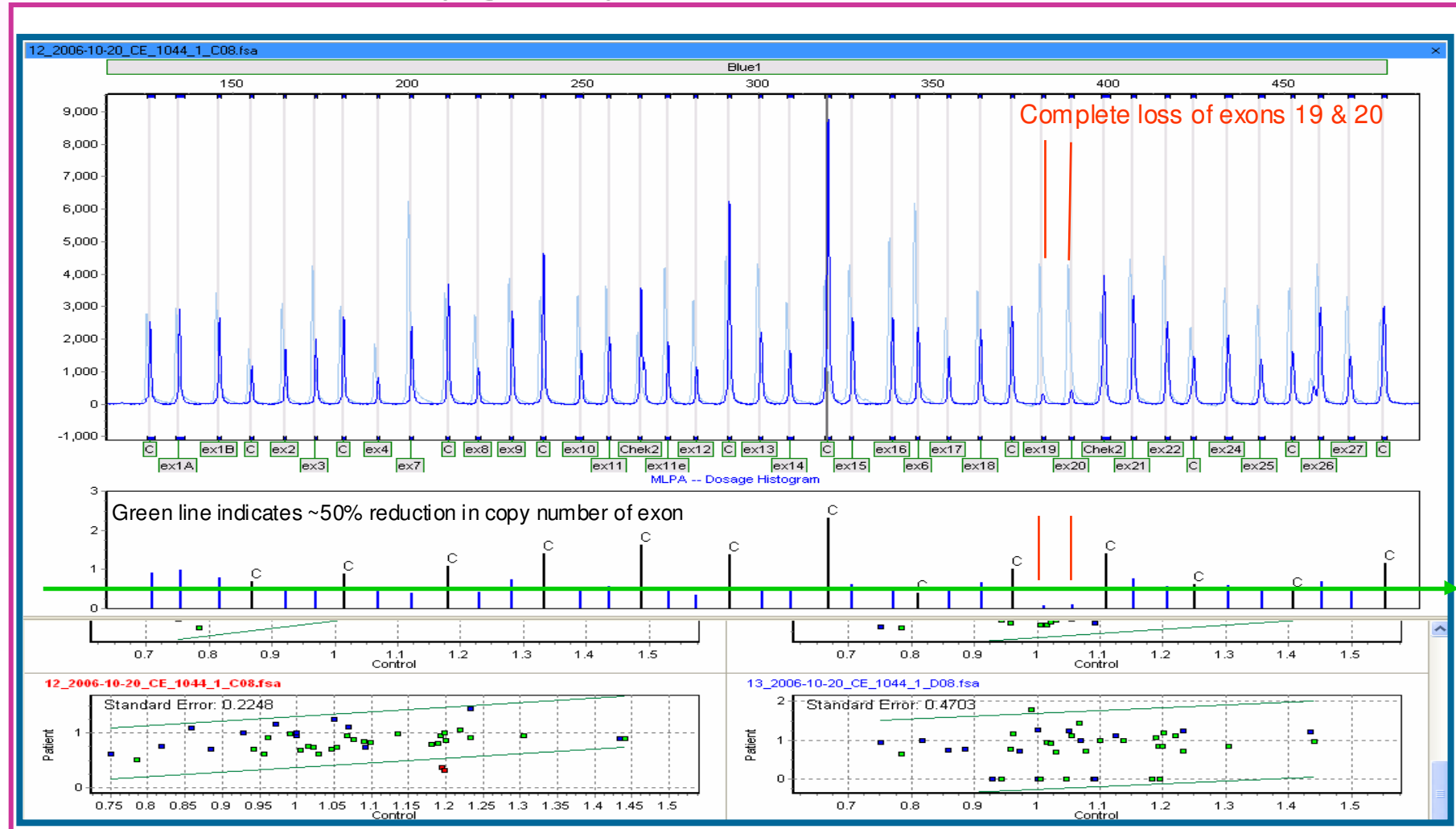
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Loss of Heterozygosity at *BRCA2* mutation locus



***BRCA2* del exons 19_20**

Light blue trace: negative control (i.e. no genomic rearrangements)
 Dark blue trace: case 12

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Outcomes:

This is the first study to show a cause and effect relationship between pathogenic *BRCA2* mutations and the development of prostate cancer

→ In 71% of cases, *BRCA2* is functioning as a tumour suppressor gene and is the cause of prostate cancer

BRCA2 mutation carriers have a younger age of diagnosis, yet slightly higher Gleason score than *BRCA1* carriers

Men from high-risk breast/ovarian families who carry a pathogenic *BRCA2* germline mutation are at increased risk of developing prostate cancer (3.5-fold).

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Future Studies (Prostate Cancer):

New research team of 10 medical professionals – urologists, scientists, medical oncologists and pathologists.

5 new aims – exploration into the molecular genetics of prostate cancer

Increased number of men in the study via an international collaboration with the Royal Marsden Hospital, London.

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Additional Research from kConFab Resource:

- Melanoma (Graham Mann)
“Genes that influence susceptibility to both breast cancer and melanoma”
- Endometrial Cancer (Amanda Spurdle)
“Endometrial cancer genetics”

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In Conclusion:

Since 1997 kConFab has:

- Established a rich/comprehensive collection of data
- Collected thousands of biospecimens
- Verified ALL cancers
- Extensive pathology review

→ Valuable biobank/data repository for future research into oncology related research:

- Prostate Cancer (International Collaboration)
- Melanoma (Graham Mann)
- Endometrial cancer (Amanda Spurdle)
- Australian Sarcoma Study (David Thomas)

kConFab's core work will continue to facilitate cancer research through access to biological samples and data.

Acknowledgements

Prostate cancer study:

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- * John Hopper -The University of Melbourne
- * Alessandro de Luca & David Huntsman - Cancer Agency, British Columbia, Canada

kConFab:

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- * Executive committee and kConFab members
- * kConFab Laboratory, Data Manager and Research Nurses

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