## **BIORESOURCE PAPER**

## The Brisbane Breast Bank

Amy E. McCart Reed<sup>1</sup>, Jodi M. Saunus<sup>1</sup>, Kaltin Ferguson<sup>1</sup>, Colleen Niland<sup>1</sup>, Peter T. Simpson<sup>1</sup> and Sunil R. Lakhani<sup>2</sup>

<sup>1</sup> The University of Queensland, Centre for Clinical Research, QIMR Berghofer Medical Research Institute, AU

<sup>2</sup> The University of Queensland, Centre for Clinical Research, Pathology Queensland, AU

Corresponding author: Amy E. McCart Reed (amy.reed@uq.edu.au)

The Brisbane Breast Bank (BBB) was established in 2005 with a view to collecting surplus tissue from every breast surgery patient at the Royal Brisbane and Women's Hospital. This not-for-profit biobank provides resources on a collaborative basis, supporting local, national and international studies. The resource prides itself on its comprehensive clinico-pathology sample annotation. Since its inception, the remit of the BBB has expanded to the prospective collection of serial blood samples from patients at high risk of recurrence, and the collection of blood and tumour tissue from metastatic patients.

**Keywords:** Breast cancer; FFPE; frozen; metastasis; Tissue microarray **Funding statement:** RBWH Foundation Diamond Care Grant/QIMR Berghofer grant, 2014–2015. National Health and Medical Research Council (NHMRC) Program grant funding: 2007, APP006598; 2012, APP1017028; 2017, APP1113867. National Breast Cancer Foundation (NBCF) Infrastructure grant, IF-14-01, 2015.

## (1) Bioresource Overview

## **Project description**

The Brisbane Breast Bank (BBB) was initiated to support high quality clinical research projects in the breast cancer field. The bank operates from the University of Queensland Centre for Clinical Research (UQCCR), located alongside the Royal Brisbane and Women's Hospital (RBWH) on the Metro North Health Services campus in Herston. The RBWH is the largest tertiary referral hospital in Queensland, providing specialist services to patients throughout the State (current population 4.84 million, approximately 20.3% of the Australian population, of which approximately 48.5% resides in the greater Brisbane area [1]). The RBWH also receives referrals from northern New South Wales, the Northern Territory and neighbouring countries in the South West Pacific.

The BBB aims to collect samples from every consenting breast surgery patient undergoing treatment at the RBWH. To this end, tumour tissue surplus to diagnostic requirements is snap frozen and banked, as well as being formalin-fixed and paraffin-embedded (FFPE) for longerterm storage and detailed histopathology annotation. This includes samples with benign, pre-invasive and invasive diagnoses. A blood sample is also taken at the time of surgery, and processed into various derivatives (serum, plasma, whole blood, buffy coat, Guthrie card). We also collect breast tissue from healthy donors undergoing reduction mammoplasty (cosmetic cases from The Wesley Hospital) and prophylactic mastectomy. The BBB is unique in that it provides highly detailed curation of the banked tissue samples. Indeed, from each banked piece of tissue a section is cut and the histology reviewed by a pathologist. To this end, we can provide reliable information about a sample's tumour cellularity, and true content of the specific piece of tissue to be supplied for research.

The BBB has supplied tumour samples to a host of targeted projects (e.g. [3-6]), as well as a sigbody of ongoing work. Importantly, nificant BBB samples made up 10% of the total breast cancer samples studied by the International Cancer Genome Consortium (ICGC), resulting in several landmark studies ([2] and refs therein). Its growing normal breast tissue resource has been used in large consortia-based studies (e.q. [7]) as well as normal breast biology projects (e.g. [8]). The recent expansion to collection of metastatic deposits has underpinned ground-breaking work characterising the genome and transcriptome of brain metastases [9]. The BBB is currently conducting a longitudinal, prospective study (Circ.BR, Circulating Biomarkers of Relapse in Breast Cancer), involving the collection of serial blood samples, primary tumour tissue and a Quality-of-Life survey from selected RBWH patients at a high risk of disease recurrence or spread. Finally, it also operates as the Brisbane node of the National Breast Cancer Foundation (NBCF)funded BROCADE (BReast Origin CAncer tissue DonatEd after death) rapid autopsy program.

McCart Reed et al: The Brisbane Breast Bank

## Classification (1) Human.

**Species** Homo sapiens.

## Classification (2)

biological samples and clinical data (where possible), including pathology, therapeutic intervention, disease recurrence and outcome.

## Context

## Spatial coverage

Description: Brisbane, Queensland, Australia.

Royal Brisbane and Women's Hospital, Herston, Brisbane. The Wesley Hospital, Auchenflower, Brisbane.

Northern boundary: -27/153 Southern boundary: -27/-152.99

## Temporal coverage

The start date of the collection period for the bioresource was 2005, and the collection is ongoing.

## Temporal coverage for accessibility N/A

N/A

## (2) Methods

## Steps

- BBB donors are recruited at the time of diagnosis of breast cancer, through the breast cancer clinic at the RBWH; or by surgeons in either the normal (reduction mammoplasty) or metastatic setting. Informed consent is required, and consent forms are managed and retained by the BBB according to standard operating procedures (SOP).
- Hospital staff or BBB staff collect blood, which is processed and stored according to a SOP.
- Tissue is couriered by BBB staff from surgical theatre to the pathology department, and where there is tissue surplus to diagnostic requirements, the BBB will collect and bank according to SOPs.
- Patient information, clinical and pathology data is collected from pathology reports and medical records, and this data is stored alongside sample information in a secure SQL database (Caisis). Unique de-identifying codes are applied to the specimens; and are also recorded in the limited-access database. Data management and auditing occurs according to SOPs.
- Experimental data is recorded for each sample, and thus integration of layers of information is possible, especially for those samples subjected to genomic analysis.
- Samples are shipped by licensed providers in accordance with I.A.T.A., UN and CASA standards.
- The BBB is integrated with other biobanks nationally through The Australian Breast Cancer Tissue Bank (ABCTB) ([10]).

## Stabilization/preservation

Blood is collected in  $2 \times EDTA$  and  $1 \times clot activator tube.$ 

Tissue is collected and couriered in sterile pots, then frozen in barcoded cryovials.

## Type of long-term preservation

Formalin-Fixed Paraffin-Embedded (FFPE), frozen, viable frozen.

All frozen samples are barcoded and de-identified; and stored in temperature monitored freezers and liquid nitrogen dewars protected by swipe card access.

## Storage temperature

Room Temperature (20°C): FFPE blocks; Guthrie cards. –80°C: DNA, whole blood, and blood derivatives. –196°C: tissue.

# Shipping temperature from patient/source to preservation or research use

e.g.  $-170^{\circ}$ C to  $-190^{\circ}$ C (liquid nitrogen dry shipper; snap frozen tissue);  $-80^{\circ}$ C (on dry ice; tissue);  $0-4^{\circ}$ C (on ice; tissue); room temperature ( $18-25^{\circ}$ C; blood samples).

## Shipping temperature from storage to research use

Dependent on tissue derivative;  $-56^{\circ}$ C (on dry ice; frozen tissue);  $0-4^{\circ}$ C (on ice; blood, DNA); room temperature (18-25°C; FFPE block).

## Quality assurance measures

Detailed pathology review performed on each banked piece of tissue, affording the BBB of level of histological curation unmatched by other local and international banks.

Standard methods of nucleic acid extraction, qualification and quantification, including by Qubit analysis and Bioanalyser, where appropriate.

The BBB's standard operating procedures have been submitted to ISBER (International Society for Biological and Environmental Repositories), and to the Australasian Biospecimen Research Network. The BBB is certified through the NSW Biobanking certification program, which is based on the Canadian process developed by the Office of Biobank Education and Research (OBER), University of British Columbia (UBC) and the Canadian Tissue Repository Network (CTRNet).

## Source of associated data

Associated data is manually collected from hospital medical records, AUSLAB (pathology information database), MOSAIQ (radiology oncology database), and CHARM (oncology database) and the Queensland Cancer Registry. Data is audited by cross-referencing, and regular manual checks.

## **Ethics Statement**

The BBB operates fully within the remit of ethical approval from the Royal Brisbane and Women's Hospital (RBWH; 2005/022 Molecular Pathology and Genetic Sub-Classification of Precancerous and Cancerous Breast Lesions) and The University of Queensland (UQ; 2005000785 Molecular Pathology of Breast Cancer).

Additional site-specific ethics approval for the BROCADE autopsy study is covered under HREC/15/QRBW/547.

The patient consents to unspecified future research on their donated sample, allowing genetic analyses as well as more long-term projects such as xenografts.

## Constraints

N/A

## (3) Bioresource description

**Object name** Breast Cancer.

**Bioresource name** Brisbane Breast Bank. Bioresource acronym or short name: BBB

## **Bioresource** location

The University of Queensland Centre for Clinical Research (UQCCR), Building 71/918 Royal Brisbane and Women's Hospital Herston, QLD 4029, AUSTRALIA.

## Bioresource contact

Kaltin Ferguson k.ferguson2@uq.edu.au.

## **Bioresource URL**

https://clinical-research.centre.uq.edu.au/lakhani-group.

Identifier used N/A

**Bioresource type** Breast cancer.

**Type of sampling** disease based.

**Anatomical site** Breast. Metastatic lesions.

**Disease status of patients/source** Breast cancer.

## Clinical characteristics of patients/source

Pre- and post-menopausal breast cancer patients. Male breast cancer.

No exclusions on the basis of treatment regime.

Samples generally collected at first surgical resection, however recurrences and metastatic lesions are also banked.

## Size of the bioresource

As at April 2017, there are 2167 consented donors.

## Vital state of patients/source

Alive and post-mortem.

**Clinical diagnosis of patients/source** Breast Cancer.

## Pathology diagnosis

Normal breast, pre-invasive and invasive lesions are collected. ICD50.

## **Control samples**

Normal breast tissue harvested from reduction mammoplasty. Distant cancer-associated normal tissue. Blood.

## Biospecimen type

Frozen tissue: 5 mm<sup>3</sup> per cryovial, number dependent on tissue size; ~50% of donors;
FFPE archival blocks: number dependent on tissue size;
Blood: Whole blood, 1 vial (0.5 ml).
Serum, 3 cryovials; 1 ml/vial.
Plasma, 5 cryovials; 1 ml/vial.
Buffy coat, 2 cryovials; 1 ml/vial.
Guthrie (dried blood spot) card; 1 card with 5 spots.

## Release date

2005.

## Access criteria

Samples are made available following a presentation of the proposed project to the BBB operating committee (as per author list). The BBB operates without cost recovery, and as such each supported proposal is considered a collaborative research project. Restrictions include whether the bank can provide sufficient samples to ensure a statistically robust experiment can be executed; whether the proposed project is unique and likely to produce significant advances in knowledge or clinical practice, making best possible use of the samples; and when there is deemed to be no conflict of interest.

## (4) Reuse potential

A non-exclusive approach is taken towards sample provision and thus samples from the same donor may be supplied for use in multiple projects. The collaborative approach taken to research agreements enhances the re-use potential of the banked samples, as detailed records for the various experiments per sample are kept and therefore extra data is able to be shared where appropriate. To date, the BBB has supplied materials to 14 internal and 15 external projects. Samples are provided at a proportion of 13% of banked tissue and 19% for blood, to both domestic and international researchers.

## Acknowledgements

In kind pathology support from Pathology Queensland (PQ): PQ Registrars (2008- present) and A/Prof Margaret Cummings.

RBWH Breast Unit: Alison McClintock, Tenille Hibberd, Prof Owen Ung, Dr Ben Green, Dr Kowsi Murugappan, Dr Clement Wong.

Other leading investigators on funding applications: Prof Owen Ung, Prof Lindy Jeffree, Prof Liz Kenny, Prof Georgia Chenevix Trench, Prof Kum Kum Khanna, Dr Alex Swarbrick, Prof Robin Anderson. Previous BBB manager: Dr Mythily Mariasegaram.

All members of the Molecular Breast Pathology laboratory, past and present.

Patients who have kindly consented to the collection of tissue, blood and clinical data for use in medical research.

## **Competing Interests**

The authors have no competing interests to declare.

#### Authors Contribution

Amy E. McCart Reed and Jodi M. Saunus have made an equal contribution.

## Author Roles

Amy E. McCart Reed: Curator/co-supervisor.

Jodi M. Saunus: Curator/co-supervisor.

Kaltin Ferguson: Collector of Data or Samples and Bioresource Manager.

Colleen Niland: Collector of Data or Samples.

Peter T. Simpson: Curator/co-supervisor.

Sunil R. Lakhani: Creator and Director.

## References

- 1. Australian Bureau of Statistics Regional Population Growth, Australia 2015–2016 2017 (cited 2017 30/03/2017).
- Nik-Zainal, S, et al. 2016 Landscape of somatic mutations in 560 breast cancer whole-genome sequences. *Nature*, *534*(7605): 47–54. DOI: https://doi. org/10.1038/nature17676
- 3. **Al-Ejeh, F,** et al. 2014 Kinome profiling reveals breast cancer heterogeneity and identifies targeted therapeutic opportunities for triple negative breast

cancer. *Oncotarget, 5*(10): 3145–58. DOI: https://doi. org/10.18632/oncotarget.1865

- 4. Vargas, A C, et al. 2012 Gene expression profiling of tumour epithelial and stromal compartments during breast cancer progression. *Breast Cancer Res Treat, 135*(1): 153–65. DOI: https://doi.org/10.1007/ s10549-012-2123-4
- 5. Wiegmans, A P, et al. 2014 Rad51 supports triple negative breast cancer metastasis. *Oncotarget*, *5*(10): 3261–72. DOI: https://doi.org/10.18632/ oncotarget.1923
- McCart Reed, A E, et al. 2013 Thrombospondin-4 expression is activated during the stromal response to invasive breast cancer. *Virchows Archiv: An International Journal of Pathology, 463*(4): 535–45. DOI: https://doi.org/10.1007/s00428-013-1468-3
- 7. **Bojesen, S E,** et al. 2013 Multiple independent variants at the TERT locus are associated with telomere length and risks of breast and ovarian cancer. *Nat Genet, 45*(4): 371–84, 384e1–2. DOI: https://doi.org/10.1038/ng.2566
- Johnston, R L, et al. 2016 High content screening application for cell-type specific behaviour in heterogeneous primary breast epithelial subpopulations. *Breast Cancer Res, 18*(1): 18. DOI: https://doi.org/10.1186/ s13058-016-0681-9
- Saunus, J M, et al. 2015 Integrated genomic and transcriptomic analysis of human brain metastases identifies alterations of potential clinical significance. *J Pathol*, 237(3): 363–378. DOI: https://doi.org/ 10.1002/path.4583
- 10. **Carpenter, J,** et al. 2014 The Australian Breast Cancer Tissue Bank (ABCTB). *Open Journal of Bioresources, 1*: e1. DOI: https://doi.org/10.5334/ojb.aa

How to cite this article: McCart Reed, A E, Saunus, J M, Ferguson, K, Niland, C, Simpson, P T and Lakhani, S R 2018 The Brisbane Breast Bank. *Open Journal of Bioresources* 5: 5, DOI: https://doi.org/10.5334/ojb.33

Published: 06 February 2018

**Copyright:** © 2018 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See http://creativecommons.org/licenses/by/4.0/.

Qpen Journal of Bioresources is a peer-reviewed open access journal published by Ubiquity Press OPEN ACCESS a