Biobanking networks: why have them and what are the essential ingredients?

Anne Thompson
Overview

- Biobanks, multiple types and multiple purposes
- Biobank networks, why form them?
- Victorian Cancer Biobank as an example
  - History
  - Objectives and purpose
  - Governance and management structure
  - Operational model and funding
  - Meeting our ethical obligations
  - Products and services and accessing them
  - Achievements - collection and distribution
- Case studies
- Essential ingredients
- Conclusions
Biobanks mission statement

“The purpose of a biobank is to supply human biospecimens that are of suitable quality and with appropriate annotation (clinical information and follow up) that enables researchers to create new knowledge leading to the prevention of or improved treatment of human disease.”

Biobanking Roundtable – Summary of Discussion

NHMRC (June, 2012)
Different types of biobanks

Biobanks can vary according to

- Size and scale
  - population based, project specific
- Health status of donors
- Different research focus
  - disease specific, environmental
- Degree of data linkage
  - lifestyle questionnaires, clinical information, medical imaging, genetic data
Cancer biobanks: common characteristics

- Involve ongoing collection
- Collect and process samples removed during therapeutic procedures (blood and tissue)
- Seek tissue samples identified by pathologists as excess to diagnostic needs
- Collect for unspecified future research
- Provide access to researchers who are not the custodians
- Link specimens to clinical and research data
Why form biobank networks?

- Increase the power of research by creating a larger pool of samples
- Increase the diversity of available samples
- Reduce costs by pooling resources and benefitting from economies of scale
- Promote collaboration, locally and internationally
- Provide sample processing expertise for multi-site clinical and translational research studies
- Increase likelihood of funding

International trend towards networking biobanks because they
## Cancer biobanks, networks and associations

<table>
<thead>
<tr>
<th>Type of structure</th>
<th>Example</th>
<th>Focus</th>
<th>Collection sites</th>
<th>Processing sites</th>
<th>Storage sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual</td>
<td>Cancer Society Tissue Bank, Christchurch, NZ</td>
<td>Cancer and other diseases; project specific</td>
<td>Single</td>
<td>Single site</td>
<td>Single site</td>
</tr>
<tr>
<td></td>
<td>Wesley-St Andrews Research Institute Tissue Bank, Brisbane, Aus</td>
<td>Cancer and other diseases; project specific collections</td>
<td>Single</td>
<td>Single site</td>
<td>Single site</td>
</tr>
<tr>
<td>National, single focus</td>
<td>kConfab, Peter Mac</td>
<td>Familial cancers</td>
<td>Multiple</td>
<td>Single site</td>
<td>Single site</td>
</tr>
<tr>
<td>National, merged</td>
<td>ALLG, Australia</td>
<td>Blood cancers</td>
<td>Multiple</td>
<td>Multi site</td>
<td>Single site</td>
</tr>
<tr>
<td>collections, single</td>
<td>APRC, Australia</td>
<td>Prostate cancers</td>
<td>Multiple</td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
<tr>
<td>focus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State based, consortium</td>
<td>Victorian Cancer Biobank</td>
<td>All cancer types; services; project specific collections</td>
<td>Multiple</td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
</tbody>
</table>
## Cancer biobanks, networks and associations

<table>
<thead>
<tr>
<th>Type of structure</th>
<th>Example</th>
<th>Focus</th>
<th>Collection sites</th>
<th>Processing</th>
<th>Storage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virtual networks, data and infrastructure sharing</td>
<td>TubaFrost</td>
<td>All cancers</td>
<td>Multiple databases</td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
<tr>
<td>Biobanking and Biomolecular Research Infrastructure, EU</td>
<td>Biobanking and Biomolecular Research Infrastructure, EU</td>
<td>Multiple diseases</td>
<td>Multiple banks and databases</td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
<tr>
<td>Service providers</td>
<td>Genetic Repositories Australia</td>
<td>Service for cell line preparation</td>
<td>Multiple</td>
<td>Single</td>
<td>Single</td>
</tr>
<tr>
<td>Associations, professional societies</td>
<td>ABNA, Australia</td>
<td>• Share expertise and promote communication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Canadian Tissue Repository network</td>
<td>• Strengthen harmonisation of policies and procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ISBER, International</td>
<td>• Highlight importance of governance and ethics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ESBB, International</td>
<td>• Develop education and training resources</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Challenges associated with forming networks

- National differences in ethics and privacy policies
- Diverse funding agencies with different priorities
- Sense of “ownership” of samples
- Agreement on storage location(s)
- Agreeing on access by members and third parties
Best practice in biobanking

Biobanks and networks must meet international best practice

• Rationale for establishment – type of research, nature of participants
• Sound governance and management structure
• Compliance with state & national legislation and ethical guidelines
• Harmonisation with international guidelines, policies and procedures
• Agreed range of biobank activities - samples collected & services to be provided
• Defined data set and whether obtained by linkage or manual entry
• Type of consent – DNA/GWS sequencing, cell line preparation, approval for future unspecified research
• Access management (process/academic/commercial)

Biobanks Information Paper, NHMRC (2010)
Establishing the Victorian Cancer Biobank

Timing

Researcher needs

• Increase the availability of large numbers of biospecimens

• Ensure specimens were of high quality

• High quality associated data

• Provide better support for the collection and banking for multi-site clinical trials

Government needs

• Increase expertise in molecular pathology and address shortage of trained pathologists in Victoria

• Support and expand the development of the biotechnology sector in Victoria
Establishing a network takes time

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Victorian government announces 5 year commitment to STI Grant Scheme</td>
</tr>
<tr>
<td>2001</td>
<td>Cancer Council Victoria (CCV) Committees recognised the need for large scale tissue banking</td>
</tr>
<tr>
<td>2002</td>
<td>Working Group formed, including existing Tissue Banks</td>
</tr>
<tr>
<td>2003</td>
<td>Project Officer (CCV) begins coordinating the development of common protocols (SOPs and PIS/CF) across 4 existing tissue banks</td>
</tr>
<tr>
<td>2005</td>
<td>Business Plan developed and funding application submitted</td>
</tr>
<tr>
<td></td>
<td>Science, Technology and Infrastructure Grant awarded by Victorian government</td>
</tr>
<tr>
<td></td>
<td>Funding Agreement signed</td>
</tr>
<tr>
<td>2006</td>
<td>June: Consortium Agreement signed</td>
</tr>
</tbody>
</table>
History and objectives

• 5 member not-for-profit Consortium formed in 2006
• Consortium brought together 4 of Melbourne’s largest tissue banks located in large hospitals
• All hospitals are adjacent to research institutions and include university medical departments
• Funded by the Victorian state government to
  • Streamline access to high quality annotated biospecimens by researchers in academia and industry
  • Reduce duplication of resources for collection and administration
  • Enable research and training in tissue based molecular patholog
  • Promote translational research collaborations locally, nationally and internationally
  • Support and link with national and international tissue banks
Role of the Business Plan

Benefits

• United Consortium members by jointly defining short-term and long term goals

• Ensures all requirements for ‘Best Practice’ will be met

• Provides reassurance to government/funding agency regarding use of funds

Content

• Objectives and outcomes

• Governance and management structure

• Financial details: analysis, costings and projections

• Milestones to measure outcomes
Role of the Agreements

Government Agreement
- Committed the government to providing funding
- Defined milestones and outcomes to be achieved

Consortium Agreement
- Members agreed to custodianship of samples being centralised
- And decisions regarding collection and access be made by the Consortium Committee
- Funding would be allocated by the Consortium Committee

Program Agreements
- Allocated funds to each member site for staff to collect process and store samples
- Set agreed targets
Governance

Consortium committee

- Structured to allow representation from all Consortium Members and ensure independent legal, ethical advice and patient/donor advocacy
- Sets the strategic direction
- Provides financial oversight and accountability to funding agencies
- Supports the Executive Officer in implementing the Business Plan

Central Sub Committees

- Report and make recommendations to the Consortium Committee
- Access Committee, oversees supply of samples to ensure appropriate use and ethical compliance; provides advice to Consortium committee on access
- Informatics Committee, provides advice on the IT platform
Governance

Member Tissue Bank Management Committees

- Provides advice on local issues to the Consortium Committee
- Terms of Reference set in agreement with Consortium Committee;
- Provide strategic and financial oversight at their site
- Supports local Tissue Bank Manager
Management

CEO/Manager

- Appointed by and reports to Consortium Committee
- Responsible for the program and stakeholder relationships
- Manages central staff

Centralised staff

- Administration and Communications Officer
- Applications Manager
- Operations Manager

Tissue Bank Managers Advisory Group

- Advise central operations staff on collection and distribution matters
- Manage relationships with clinicians and researchers locally
Governance and Management

Two-tiered structure
Consortium members

Pre-existing tissue banks

- Austin Health
- Melbourne Health
- Peter MacCallum Cancer Centre
- Southern Health
- Cancer Council of Victoria (Lead Agency)

- 27 associate members
  - research institutes, private pathology providers; private hospitals
Operational model

- Unique centralised process for access to biospecimens and services
- Organised in a “hub and spokes” structure with
  - Number of processing sites = 8
  - Number of storage sites = 4
  - Number of collection sites = 27
Location of sites

- Population of Australia – 21.4 million
- Population of Victoria – 5.3 million
- Metropolitan Melbourne – 3.9 million

Source: Australian Bureau of Statistics, June 2008
Funding

Victorian Government

**Phase I: Science Technology and Infrastructure (STI-3) Grant**
- 2006 - 2009, $7 million to establish and fund the operational model
- Members and associates committed to providing an ‘In-kind’ contribution of equal value

**Phase 2: Victorian Cancer Agency**
- 2008 – 2012, $8.33 million
  - For maintaining collection and distribution and expanding to regional areas; maintaining ICT capabilities; expanding support for clinical, translational and project specific research
  - Purchase and install digital imaging equipment ($1.23 million) at 4 Consortium member sites
Funding, 2012/13

Victorian Government

May 2012 Budget commitment

• $14.9 million per annum to support translational research in Victoria through the Victorian Cancer Agency, recurrent

• A key focus of the Agency is the development of an integrated cancer research platform that builds on and links existing cancer research infrastructure including data platforms

• Biobank considered a key component of the platform

• $2.23 million provided for us to better position ourselves for the integration
Ethics obligations

Biobank must comply with

• National Statement on Ethical Conduct in Human Research (March 2007) (National Statement)

• Human Tissue Act 1982 (Vic) and Coroners and Human Tissue Acts (Amendment) Act 2006 and Regulations (Regulation 6)

Compliance ensured by 2-tiered approval process

• Biobank has approval from 13 HRECs to approach donors at 27 hospitals using PIS and CF

• Researchers must demonstrate approval for their research using human tissue or an exemption certificate

• Biobank has ensured donors and HRECs that tissue will only be supplied for approved research
Patient Information Sheet

Ensures donor is fully informed of

- Purpose of the research (unspecified future research)
- What participation involves - blood donation and access to surplus surgical material
- Risks and benefits (if any)
- Oversight of use in future unspecified research - ethical approval/review
- Security of and access to stored tissue and data
- Responsible host organisation and custodian
- Managing medically significant findings
- Right to decline or withdraw
Donor Consent Form

Please read carefully and tick either YES, NO or NA (Not Applicable)

1. I give permission to have 25–50ml of my blood collected.
   - YES  NO

2. I give permission for an additional 25–50ml of blood to be collected at follow up visits.
   - YES  NO

3. I give permission for cells obtained from my blood or tissue to be used to establish cell lines. (A cell line is comprised of cells that have been allowed to grow indefinitely.)
   - YES  NO

4. You may use my samples to conduct studies that identify genes or diseases that run in families, for example, diseases that can be passed on (through DNA) to blood relatives.
   - YES  NO

5. I give permission for health information to be collected from my doctor, medical records or through ethically approved health databases or cancer registries.
   - YES  NO

6. You may use my archived tissue paraffin (wax) blocks for research.
   - YES  NO

7. You may contact me in the future to take part in other research projects or surveys.
   - YES  NO

8. I give permission to have an additional 10mls of bone marrow collected.
   - YES  NO  NA

9. I give permission for bone marrow to be collected at follow up visits.
   - YES  NO  NA

If an Interpreter was used, please fill in the following:

Interpretation:
I have interpreted the Patient Information Sheet and Consent Form to the above in a language he/she may understand.

Interpreter’s Name (print):  Signature:  Date:
Products and services

- Archival biospecimens
  - Frozen or embedded tissue (OCT and paraffin)
  - Snap frozen tissue
  - Serum, plasma, PBMNCs
- Fresh tissue
  - From pathology to researcher within 3 hours
- Clinical research support
- Project specific collection
- Value added services
  - DNA, RNA and tissue microarray preparation
Digital imaging service

- Slides stained
  - H&E
  - IHC

- Slides scanned
  - 120 slides per rack
  - <1 min per slide

- Slide images stored
  - 750 Mb per slide

- Separate “spot images” viewed
Architecture

Spectrum Local (Client)

Biobank sites (4)

Aperio Scanner
Scan Scope
Image Server
LAN
Image Scope
Image Scope

Spectrum Collaboration (Central Server)

Biobank Central and External Collaborators

IP Sec Router
Image Scope
VPN Links

IP Sec Router
Central Server

VPAC
Image Server
Providing training and quality biospecimens

### Pathology Verification

**SPECIMEN ID**

**LAB:** [Redacted]  | **DATE:** [Blank]

**Surgical Site (organ):** [Blank]

**Primary Tumor Site (histology):** [Blank]

**Pathology Report Diagnosis:**

- (Carcinotype) [Blank]
- (Subtype/no subtype) [Blank]
- (Grade) [Blank]

**TUMOUR SLIDE**

- Tissue preservation: Yes
- Concomitant with diagnosis: Yes
- Suitable for IHC preparation: Yes
- Suitable for TE preparation: Yes
- Suitable for Use: Yes

**Comment:** [Blank]

#### Neoplastic Component

- Invasion:
  - Scleroma: [Blank]
  - Necrosis: Yes
  - Infiltration: Yes
  - Dystrophy: Yes
  - Metaplasia: Yes
  - Lymphoid/ Vascular Invasion: Yes
  - Parasitic Invasion: Yes

**Normal Component**

- Epithelium: Yes
- Parathyma: Yes

**Comment:** [Blank]
Streamlined Approval Process

1. Research projects obtain HREC approval
2. Download forms from website, complete and submit to the Applications Manager
3. Access Committee review
4. If approved an agreement is put in place
5. Biospecimens dispatched or service commenced with one month
Materials Transfer Agreement

- Life of human tissue products extends from collection through processing into biospecimens
- Ensures compliance occurs following transfer of biospecimens to researchers by
  - Between biobank and researcher institution
  - Specifies use of materials and includes any derivative
  - No transfer to a third party
  - Biobank retains ownership of materials; organisation owns intellectual property rights
Service Agreement

- Used for clinical research or trials where protocol differs from VCB standard and is not standard of care
- Study specific PIS and CF is used
- Consent obtained by study staff if drug is being administered
  - Between biobank and researcher institution or study sponsor
  - Sponsor has ownership/custodianship of materials
  - Sponsor owns intellectual property rights
International supply

Compatibility Issues
• Consent for unspecified future research
• HRECs do not recognise need for 2-tiered approval process
• Individual HRECs in Australia interpreting NS differently

Safeguarding Australian donors
• Places increased importance on the informed consent process for GWS and unspecified future research

Certainty essential for international collaborative research
Achievements - donor support

Collection targets

- each site exceeded agreed annual targets (>3000 donors per year)
- Donor altruism based on desire to improve cancer diagnosis and treatment for others
Achievements - all tumour types

- Largest biobank in Australia that collects all tumour types
- > 350,000 blood and tissue samples stored
- Predominantly colorectal, breast and prostate tissue products

* Other = ‘benign’ tissue (eg. Thyroid nodules)
Supporting research

- 138 applications received by June 2012
- 34 projects fully supplied and closed
- 57% for archival biospecimens
- 15 clinical trials/clinical research projects supported
- Samples provided to
  - 7 international research groups (5 USA)
  - 9 interstate
  - 116 local groups (8 fresh tissue)
- 28,893 samples dispatched from Jan 2007 to Dec 2011
Biospecimens and services:

October 2007 – December 2011

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Tissue Biospecimens</th>
<th>Blood Biospecimens*</th>
<th>Value Added</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fresh Tissue</td>
<td>Snap Frozen Tissue</td>
<td>FFPE / OCT Sections</td>
<td>FFPE / OCT Blocks</td>
</tr>
<tr>
<td>CNS</td>
<td>1</td>
<td>19</td>
<td>545</td>
<td>-</td>
</tr>
<tr>
<td>Breast</td>
<td>1,028</td>
<td>526</td>
<td>2,965</td>
<td>1</td>
</tr>
<tr>
<td>Colorectal</td>
<td>14</td>
<td>2,412</td>
<td>5,765</td>
<td>455</td>
</tr>
<tr>
<td>Genitourinary*</td>
<td>79</td>
<td>40</td>
<td>1,692</td>
<td>405</td>
</tr>
<tr>
<td>Gynaecological</td>
<td>112</td>
<td>9</td>
<td>75</td>
<td>4</td>
</tr>
<tr>
<td>Haematological**</td>
<td>6</td>
<td>-</td>
<td>190</td>
<td>-</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>47</td>
<td>97</td>
<td>1,876</td>
<td>-</td>
</tr>
<tr>
<td>Lung</td>
<td>156</td>
<td>6</td>
<td>579</td>
<td>246</td>
</tr>
<tr>
<td>Skin (Melanoma)</td>
<td>143</td>
<td>38</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>Upper GI****</td>
<td>76</td>
<td>76</td>
<td>613</td>
<td>-</td>
</tr>
<tr>
<td>Other****</td>
<td>-</td>
<td>115</td>
<td>252</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1,662</td>
<td>3,335</td>
<td>14,374</td>
<td>1,111</td>
</tr>
</tbody>
</table>
A. Large inventory enables translational research
Protein biomarkers in colorectal cancer
(LICR Parkville, CSIRO and others)
- Phase 1 - from 2005, 300 serum and plasma samples (150 CRC and 'normal' donors) sent to CSIRO Adelaide for analysis
- 50 potential biomarkers identified
- Phase 2 - commenced 2011, donors prospectively accrued from colonoscopy clinics; blood collected, processed, sent to CSIRO Adelaide

B. Supporting international collaborations
Clinical Lung Cancer Genome Project
(SVH, Peter Mac, Max Planck Institute)
- Mr Gavin Wright and Dr Ben Solomon develop a collaboration with clinicians at Max Plank Institute
- 224 samples from Australian donors provided from all VCB sites
- Largest international contribution
- Amplified FGFR-1 detected in 20% of SCC patients
- Available therapy being tested in patients

C. Network of clinicians and skilled staff enables translational research
ICGC Pancreatic Study - Australia
(Prof Andrew Biankin, Garvan Institute, Sydney)
- No Victorian PIs; Victorian surgeons wanting to support project
- Genome wide methylation patterns to be analysed in 375 pancreatic cancer samples
- VCB network of skilled staff to collect and process samples and data according to international protocol
- Pilot commenced at Austin; expansion to other sites in 2012
Essential ingredients

• Create unity by ensuring all participating groups are included in decision making through a sound governance and management structure
• Accept that sometimes decisions will be made that will undo the sense of inclusion
• Clearly define and document objectives, to ensure the vision is shared by members and clearly understood
• Document all policies and procedures so that agreed expectations are clear
• Accept that objectives will change as the network evolves and the needs of the scientific community changes
• Regularly review strategies to achieve the objectives
• Establish IT infrastructure to support the management of the collection, ensure samples are accurately annotated and streamline access
Conclusions

Integrated biobank networks can be successfully formed and will provide significant benefits to researchers and the community.