Biobanking for research meets the workflow of a diagnostic pathology laboratory

NSW Health Pathology Pilot Project

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Kolling Institute
Creating strong links between hospital diagnostic & hospital/university/institute research laboratories to support biobanking for research
Kolling Institute Tumour Bank (KITB)

~ 30,000 samples

~ 9,400 patients


Endocrine
adrenal parathyroid thyroid

Upper GI
gastric liver oesophageal pancreas

Breast
Gynaecological
cervical endometrial ovarian

Neuro
brain pituitary

Healthy Volunteers

Tumour Banking for the Future

All Tumours “global consent”
KITB Activities

Collections (current):

- Endocrine, Upper GI, Breast, Gynaecological, Neurological, “Other” (colorectal)
  
  …. our “local banks”

- Supporting external initiatives:

  - INOVATe (Individualised Ovarian Cancer Treatment through Integration of Genomics Pathology into Multidisciplinary Care)

  - Sydney 1000 Colorectal Cancer study

Consent:

- 500 ~ 700 cancer patients per annum give informed consent for their samples to be collected and stored for research, to be issued to ethically approved projects to facilitate translational cancer research

- Informed consent taken by tumour bank staff, 5 – 30 minutes
KITB Activities cont’d (2)

Samples & clinical information:

- **snap frozen tumour tissue**, adjacent normal tissue
- **FFPE blocks** – tumour tissue, adjacent normal tissue
- **blood** – whole blood, buffy coat, plasma, serum

- **processing, logging & data auditing** managed by tumour bank staff

- **collection of clinical information** managed by tumour bank staff (path reports etc.) &/or other dedicated staff (external collections)

- **storage** at the Kolling Institute in dedicated -80 freezers and vapour phase tanks, FFPE blocks at room temperature at the Kolling Institute
Issuing samples to researchers:

- tumour bank staff manage the application process
- co-ordinate panels for scientific review
- all communication with applicants, including managing MTAs
- communication with data custodians & the KITB Access Committee
- requesting & compiling data for annual reports from researchers

Ethics / Governance / Reporting:

- extensive paperwork
Pilot Project Timeline

PHASE I
Pre-intervention “business as usual”

PHASE 2A
Training & in-services

PHASE 2B
“Handover”

Tumour types in the pilot:
- breast cancer
- pancreatic cancer
- gynae cancers
- colorectal cancer

July - Aug
6 wks

Sep - Nov
12 wks

Dec - Feb
12 wks

Mar - May
9 wks

Analyses & reporting

Xmas time
Anatomical Pathology (AP) at RNSH

- **30,800 patient cases** processed through AP in 2017
  (~ 2.7% increase on 2016)

- avg. **550 FFPE blocks / day**

- ~ **143,000 FFPE** blocks per annum (260 working days)

- ~ 1 in 2 patients relate to a cancer diagnosis (other cases include inflammatory disease, renal transplants, pregnancy-related tissue …)
“Most of the world will make decisions by either guessing or using their gut. They will be either lucky or wrong.”

- Suhail Doshi, CEO, Mixpanel
Slide preparation:
Total samples banked (Phase 1 – 2B)
(~8 month period, Sep – 3/5/2018)

N = 549
(Phase I – Phase 2B, cut-off 3/5/2018)

KITB
N = 393
(72%)

WPP
N = 156
(28%)

Tumour types in KITB:
- adrenal
- parathyroid
- thyroid
- gastric
- liver
- oesophagus
- brain
- pituitary
- cervical
- endometrial

Tumour types in WPP:
- breast
- pancreatic
- ovarian
- colorectal
Patients^ banked over project phases

**PHASE I**
Pre-intervention
“business as usual”

**PHASE 2A**
Training & in-services

**PHASE 2B**
“Handover”

*Sep - Nov* 12 wks  *Dec - Feb* 12 wks  *Mar - May* 9 wks

KITB  patient numbers

WPP

^ represents individual patient numbers (samples including fresh-frozen, FFPE)
Preliminary data on time impact of embedding research biobanking within a diagnostic pathology department

![Bar chart showing average time (min) for tissue acquisition and preparation per case for different roles across phases.](chart.png)

- **Phase 1**
- **Phase 2a**
- **Phase 2b**

Roles include:
- Registrars
- Biobank officer
- Technical officer
- Technical admin.
- Pathologists

Average times (min) for each role across phases:

- Registrars:
  - Phase 1: ~8
  - Phase 2a: ~8
  - Phase 2b: ~8

- Biobank officer:
  - Phase 1: ~25
  - Phase 2a: ~5
  - Phase 2b: ~5

- Technical officer:
  - Phase 1: ~5
  - Phase 2a: ~20
  - Phase 2b: ~5

- Technical admin.:
  - Phase 1: ~0.5
  - Phase 2a: ~0.5
  - Phase 2b: ~0.5

- Pathologists:
  - Phase 1: ~0
  - Phase 2a: ~0
  - Phase 2b: ~0
Factors impeding biobanking for research in a diagnostic facility

- *ad hoc* nature of requests (& protocols) to biobank specimens disrupts workflow
- lack of protocols for handling research specimens, including workflow tracking
- focus on production of FFPE blocks, not snap frozen tissue for long term storage
- minimal capacity for long term ultra-cold storage (one -80 freezer only)
- no processing of blood samples in Anatomical Pathology labs … no centrifuge, nor a space for one
- limited access to computers for logging research specimens
- pathologists are not routinely reporting on “research” blocks
- accountability for all activities to a commercial entity (NSW Health Pathology)
- inadequate (often no) funding for research activity
- lack of a biobanking presence in diagnostic laboratories
- research biobanking often seen as an “extra”, a “favour”, not part of KPIs
- frequent staff rotations (theatre staff, registrars … information retention)
Introduction of ‘tools’ to support embedding of research biobanking (1)

- In-services: 6 given at RNSH and NSP theatres
  - 1 given to pathology registrars
  - 1 given to pathology laboratory staff

- Many (many) ad hoc / impromptu conversations to implement new workflows

- Stickers for path request forms in theatre

- Information clearly displayed in cut-up areas

### Kolling Tumour Bank – Anatomical Pathology – Cut Up Guide

<table>
<thead>
<tr>
<th>BioBank Collections/ Tissue Type</th>
<th>Fresh Tissue</th>
<th>FFPE Blocks</th>
<th>Storage/Labelling</th>
<th>Contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolling Tumour Bank (Comment or sticker on Path Request form)</td>
<td>1 x 0.5cm³ Tumour Tissue</td>
<td>1 x 0.5cm³ Tumour Tissue</td>
<td>Fresh Tissue – CryoVials stored in Liquid Nitrogen Dewar – Cryostat room.</td>
<td>PH: 9925 4771 MOB: 0434 660 881 (Usha Pillai or Mikaela Holmes)</td>
</tr>
<tr>
<td></td>
<td>1 x 0.5cm³ Normal Tissue away from Tumour (CryoVials on small cut bench)</td>
<td>1 x 0.5cm³ Normal Tissue away from Tumour (Both in 1 x Block) (Cassettes on big cut bench)</td>
<td>FFPE blocks/H&amp;E Slides Stored at workbench in Research tray.</td>
<td>Kolling Tumour Bank (Mon – Fri 9am – 4:30pm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Block/ CryoVial Label → Patient MRN/P#</td>
<td></td>
</tr>
<tr>
<td>INOVATE (Ovarian Cancer)</td>
<td>1 x 0.5cm³ Tumour tissue (Tumour Bank)</td>
<td>2 x 0.5cm³ Tumour tissue</td>
<td>Fresh Tissue – CryoVials stored in Liquid Nitrogen Dewar – Cryostat room.</td>
<td>Out of hours collection: Store in Liquid Nitrogen Dewar</td>
</tr>
<tr>
<td></td>
<td>1 x 0.5cm³ Tumour tissue (INOVATE)</td>
<td></td>
<td>FFPE blocks/H&amp;E Slides Stored at workbench in Research tray.</td>
<td></td>
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<td>Block/ CryoVial Label → Patient MRN/P#</td>
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Introduction of ‘tools’ to support embedding of research biobanking (2)

- choose a colour palette for biobanking
- pathology slide review protocol (previously no reporting on any research blocks)
Introduction of ‘tools’ to support embedding of research biobanking (3)

- inclusion of tumour bank SOPs into **Pandora** (electronic Pathology SOP database)
<table>
<thead>
<tr>
<th><strong>Research</strong></th>
<th><strong>Diagnostics</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic metrics – publications, grants, student completions, translational research</td>
<td>Patient numbers</td>
</tr>
<tr>
<td>Funding – unstable, multiple sources, limited longevity</td>
<td>Budget derived sources focussed on cost efficiency</td>
</tr>
<tr>
<td>Busy schedules, time to think, plan, read to enable high quality research</td>
<td>Busy schedules, rigid workflows to ensure high quality control … no down time</td>
</tr>
<tr>
<td>Methods are there as a basic guide. They are frequently changing, adapting rapidly with new knowledge … always improving</td>
<td>SOPs are rigidly adhered to with no chance of different interpretation of protocols. Tried &amp; proven methods based on accuracy &amp; efficiency</td>
</tr>
<tr>
<td>Many methods, multiple different experiments employed to address a range of research questions</td>
<td>Tightly honed group of methods with clear focus on efficiency and quality control</td>
</tr>
<tr>
<td>Frequent non-linearity of research path</td>
<td>Difficult to retrieve a specimen once it’s been through a checkpoint</td>
</tr>
<tr>
<td>Routine email communication facilitated by easy access to computers</td>
<td>Email communication less favoured, especially for those at the bench. More emphasis on information transfer at meetings</td>
</tr>
<tr>
<td>Capacity for long-term ultra-cold storage</td>
<td>Limited capacity for long-term storage of frozen samples, focus on FFPE blocks</td>
</tr>
<tr>
<td>Often a single researcher handling samples</td>
<td>Team approach to processing of samples, each person with a clear role</td>
</tr>
</tbody>
</table>
Significant aspects of research biobanking activities likely “un-embeddable” within diagnostic pathology laboratories

- taking informed patient consent for research biobanking
- long term ultra-cold storage of research specimens
- ethics & governance applications / renewals / reporting
- development of patient literature to accompany consent … newsletters …
- management of review of researcher applications and issuing of samples
- blood collections
- capture of long-term clinical follow-up data
Preliminary suggestions to improve research biobanking in diagnostic pathology laboratories

- **understanding of the local factors** driving both research and diagnostic environments and how to better work together to achieve common and distinct goals.

- Work with diagnostic labs to **establish protocols & other “tools” that can be embedded** into routine diagnostics with minimal disruption … avoid an *ad hoc* approach.

- Requirement for **dedicated biobank staff**, both within and outside of diagnostic labs to cover all tasks associated with research biobanking … lynchpin staff that merge needs of two environments.

- Recognition that there is **impact on the time** of staff employed for routine diagnostics, especially registrars … **funding mechanism** required to address this.

- **“top down” as well as “grass-roots up” approaches** are needed

  - research biobanking activity included as part of KPIs of NSW Health Pathology diagnostic labs (and adequately resourced)
Anatomical Pathology, RNSH
Antony Kaufman
Kimiko Blendell
Nathan Hall
John Turchini
David Nevell
Cameron Turner
Di Reader

Anatomical Pathology staff

Kolling Institute Tumour Bank
Ussha Pillai
Mikaela Holmes
Shannon Chan
Sam Yuen

Human Resources
Surgeons
Anaesthetists
Clinical nurse consultants
Administrative assistants
Patients

NSW Health Pathology
Kathleen Phillips
Simon Cooper
Jane Carpenter
Verity Hodgkinson

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