How Can Biobanks Best Provide Support for Translational Research?

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The Translational Circuit

Targeted drug development

Bedside

Target identification

Bench

Target identification

Targeted drug development
The Issue with Tissue

• Operations carried out in hospitals – basic cancer research carried out in Universities
• Difficult to get hold of high quality material from busy pathology departments without giving them help
• Priority given to diagnosis – but often plenty of useful research material wasted, as no funds available (Health Service or University) to curate samples
The Cancer Research Pyramid and tissue banks

- Clinical Trials
  - Human tissue
- Human tissues or organs in vitro
- Unmodified animals in vivo
- Primary human cells in vitro, genetically modified animals
- Human cells or tissue xenografts
- Human or animal cell lines, in silico models
- Fundamental Biology
Tissue banks can help with

- provision of biological material
- clinical annotation of samples
- processing of samples to derivatives (e.g. RNA, DNA, protein)
- pathology and molecular biology QA
- tracking of samples
- collation of research data on individual patients
Sample acquisition - preoperative

Pre-operative

- Core biopsies (very useful for non-operable cancers e.g. Lung)
- Blood samples
  - Whole blood – germline DNA
  - Serum/plasma
    - Circulating tumour cells/RNA/miRNA/methylated DNA
- Other bodily fluids (urine etc)
Sample acquisition - operative

- Intra-operative
  - Bile
  - Pancreatic fluid

- Operative specimen
  - Snap frozen tissue
  - Tissue stored in stabiliser
  - Fixed tissue
Patients with metastatic disease

- Blood (circulating tumour cells, DNA, RNA, miRNA)
- Metastatic biopsies
- Cells from ascites/pleural effusions
- Post mortem biopsies – particularly useful for non-clinically accessed sites e.g. brain
Cohort or population based biobanks
- prospective collection samples from all patients in a particular population

Project based biobanks
- related to a particular trial or tissue i.e. prior selection of sub-population based on clinical features
Cohort/population banks

• Consent is generic – donors not assigned to a particular study at the time sample is taken
• Requires a knowledge of the patient pathway and good interaction with clinical departments (pre-assessment clinics, surgical team, pathology department)
• Considerable administration – clinical annotation, tracking of samples and projects
Cohort/population banks - advantages

- Provides infrastructure for many projects
- Provides information on frequency of biomarkers in real patient population
- Provides mechanism to assess biomarkers in clinical pathway setting
- Can provide baseline samples from patients enrolled in clinical trials
- Can provide samples of different format during patient journey
Issues with clinical trials

• Consent for entry into a clinical trial is usually sought once the patient is known to fit the entry criteria

• Diagnostic specimens have already been taken

• Opportunity to collect bespoke specimens (e.g. Frozen/RNA later) lost by trial entry point
  – Cohort/population biobanks may hold valuable baseline samples

• Clinical trials run by oncologists – not pathologists. Often ideas of sample collection ill-informed
What can Biobanks add?

Biobankers know what it is possible to collect and in what format

• provide specimen patient information sheets, flowcharts etc

• relieve the pressure on histopathology departments to provide material for trials, and improve supply of biological material for trials

• Samples collected to SOPs – and preferably QA’d before issue to researchers
The importance of QA

The sample MUST be what we say it is

It MUST be fit for purpose
Garbage in...

Diamonds in.....

...garbage out
QA at source means that you can ensure that you utilise as much of your resource as possible, and that material is not thrown away by researchers because it does not meet their QA standards.

Keep your promise to your patients and keep your researchers happy!
Pathology QA

• Frozen and FFPE tissue blocks received, barcoded
• Section taken to confirm presence of disease
• H and E’s digitised – can be made available to researchers over the web
How much of my sample is tumour?
Tissue bank services

Tissue microarray

Extraction of DNA/RNA plus QA

Provision of processed material means better use of donations, and more opportunity to add value
Sample tracking - COIN

1700 patients
4040 blocks
In 3 years
Integrative (systems) biology

Tissue samples

Blood sample

DNA

miRNA

protein

mRNA

metabolites
Collating research results

• Multiple samples and their derivatives from single patients issued to researchers
• Annotation of remaining samples research results facilitates integrated biology research
• Caveats
  – research data must be captured in association with metadata on protocols used in research
  – the roles and responsibilities of primary and secondary researchers must be stated in material and data agreements when samples issued
Collating research results
CTB portal:
https://cisbic.bioinformatics.ic.ac.uk/ctb/html_ctb_public/
Collating research results

CTB Tissue Bank Search Filter

Remove items from your selection using the Del buttons. Items are arranged in donor order and multiple items for a single donor (for instance matched pairs) appear under each other. Once you are happy with your selection, use the button at the bottom of the page to apply for the samples and/or data.

Edit this search

Your selection now contains 244 tissue samples from 63 cases and 123 data items
Displaying the first 30 cases

<table>
<thead>
<tr>
<th>Donor ID</th>
<th>Donor Information</th>
<th>Samples Available</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>UA0249</td>
<td>Sex = Female</td>
<td>RNA : Normal tissue : Papillary carcinoma</td>
<td>Polymorphism :: Affymetrix :: Genome-Wide Human SNP</td>
</tr>
<tr>
<td></td>
<td>DOB = Before Accident</td>
<td>RNA : Tumour tissue : Papillary carcinoma</td>
<td>Copy Number :: BAC :: 1 Mb</td>
</tr>
<tr>
<td></td>
<td>Country = Ukraine</td>
<td></td>
<td>Gene Expression :: Affymetrix :: U133 Plus 2.0</td>
</tr>
<tr>
<td></td>
<td>Exposed to Radiation? = Yes</td>
<td></td>
<td>Gene Expression :: Affymetrix :: U133 Plus 2.0</td>
</tr>
<tr>
<td></td>
<td>Exposure Age = 2</td>
<td></td>
<td>Gene Expression :: Affymetrix :: U133 Plus 2.0</td>
</tr>
<tr>
<td></td>
<td>Operation Age = 16</td>
<td></td>
<td>Gene Expression :: Affymetrix :: U133 Plus 2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BRAF/RET status = known</td>
<td></td>
</tr>
</tbody>
</table>
Take home messages

• Biobanks are essential to translational research
• Transparent access policy for researchers
• Can do so much more than collect and release pieces of tissue or fluid samples
• Bioinformatic infrastructures plus tissue banks = stratified medicine
• Must be quality driven and fit for purpose
• Should be integrated with health services whenever possible
Further information

Imperial College Healthcare Tissue Bank
www.imperial.ac.uk/tissuebank

Chernobyl Tissue Bank
www.chernobyltissuebank.com

Wales Cancer Bank
www.walescancerbank.com