Biobanking: The Past, Present, and Future

Medical Oncology CE
Sept 19, 2008

Dr. Patricia Shaw
Director, PMH/UHN Biobank
Dept. of Pathology
Toronto Ovarian Tissue Bank and Database

- Samples:
  - Snap frozen tissue
  - normal
  - benign
  - LMP
  - Malignant, primary and metastatic
- Paraffin blocks and glass slides
- Ascites
- Blood
- Comprehensive database - Pathology, clinical, family history, treatment, follow up
<table>
<thead>
<tr>
<th>Stage and Histological Type</th>
<th>Stage I-II</th>
<th>Stage III-IV</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrioid</td>
<td>84%</td>
<td>16%</td>
<td>9%</td>
</tr>
<tr>
<td>Mucinous</td>
<td>77%</td>
<td>23%</td>
<td>6%</td>
</tr>
<tr>
<td>Clear cell</td>
<td>53%</td>
<td>47%</td>
<td>9%</td>
</tr>
<tr>
<td>Serous</td>
<td>6%</td>
<td>94%</td>
<td>75%</td>
</tr>
<tr>
<td><em>HGSCa</em></td>
<td>&lt;2%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TOTAL 22% 78% (749)

*Ovarian Tissue Bank and Database 1996-2006*
HISTOLOGIC FEATURES OF BRCA1/BRCA2 MUTATION ASSOCIATED CARCINOMAS

- Serous histology
- p53 overexpression by IHC 70%; mutations up to 80%
- Increased cell proliferation
- Higher stage
- Higher Silverberg grade
- No morphological distinction between BRCA1 and BRCA2 cancers
- No morphological distinction between hereditary and sporadic high grade serous carcinomas

Shaw et al 2002
## OCCULT CANCERS IN PROPHYLACTIC SALPINGO-OOPHORECTOMY SPECIMENS

<table>
<thead>
<tr>
<th>159 patients:</th>
<th>BRCA1 (94)</th>
<th>BRCA2 (64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer diagnosis at surgery</td>
<td>6 (6.4%)</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Mean age at diagnosis</td>
<td>49.5 yr.</td>
<td>53 yr.</td>
</tr>
<tr>
<td>Cancer Type</td>
<td>Serous grade 3</td>
<td>Serous grade 3</td>
</tr>
<tr>
<td>Cancer site</td>
<td>5/6 tube 3/6 ovary &amp; tube 1/6 ovary only</td>
<td>Peritoneum</td>
</tr>
</tbody>
</table>

Finch et al 2006
Carcinoma in situ

Normal mucosa

Dysplastic mucosa
A New Model for High Grade Serous Tumorigenesis

Normal → p53 Signature → TIC → HGSCa

BRCA1
Gene Expression Profiles of Luteal Phase Fallopian Tube Epithelium from BRCA-Mutation Carriers Resemble High Grade Serous Carcinoma

Tone et al CCR 2008
Genomics  Proteomics  Metabolomics

All depend on high quality annotated human biospecimens
Effects on Clinical Outcomes:
• Potential for incorrect diagnosis
  – Skewed biochemistry results
  – Altered immunohistochemistry reactions
• Potential for incorrect treatment

Effects on Research Outcomes:
• Irreproducible results
• Misinterpretation of artifacts as biomarkers
Multiple Variables Can Affect the Integrity of the Biospecimen

- Anesthesia
- Drugs
- Clamp time

• Type of tube
• Time at room temperature
• Rate of freezing
• Time in fixative
• Size of aliquots
Pre-analytical Variables

Quality of sample handling:

• Her2-neu IHC
  – Very specific instructions for use to get validated results:
    • Thickness of section
    • Formalin minimum & maximum
    • Ag retrieval and buffer

• in community there is a high false positive rate and a 20% false negative rate

• FISH (Pathvision)– if 2+ - FISH will be false negative if fixed over weekend
Effects of tissue processing techniques on biomarker analysis:

- time of post-fixation
- temp of paraffin
- section thickness,
- water bath temp
- ? ammonia
- time and temp of slide drying
- ? Baking
- ? Deparaffinize
- how to store
Tumor Content

OVARIAN CORTEX

TUMOUR STROMA

LYMPH NODE

NECROSIS
FDA is attentive to sampling issues:

- Analyte must be stable
- Descriptive info
- Sampling free from bias
- Clear scientific requirements
- Clear legal requirements – the sample is a subject – IRB and informed consent
- Guidance document “leftover specimens”:
  - Emerging issues – expression array – need to evaluate collection, transport, storage, validate, specify conditions
- If 3rd party diagnostics needed to direct therapy – very specific – the marker is as important as the drug
Perhaps you'd like to donate some of your genes to a biobank.

What's a biobank?

What am I agreeing to?
Informed Consent

• Study information
• Brief, clear language
• Address provincial and federal regulations (PHIPA etc)
• Confidentiality – de-identification
• Conflict of interest
• Disclose that discoveries that may have commercial value
• Secondary use
• Study information brochure/website link
• **Part of pre-admit package at UHN**
Access to Specimens and Data

Clear Policies for Data and Specimen Access:

- Timely, equitable, appropriate access
- Without undue administrative burden
- Cost recovery – not at PMH/UHN
- De-identification
- Data access system with defined privilege levels
- Levels of security appropriate for type of specimens
- Specific protocol requirements to be met before other access is considered
Access to Human Tissue, Blood, Body Fluids – PMH/UHN:

1. Complete Human Tissue Committee application with research plan summary
2. First submission to Site Group Tissue Committee:
   • availability of tissue
   • scientific value
   • utilization priority
3. Signature of Clinical rep & Pathology rep
4. Submit to REB Tissue Committee
5. Approval letter to Biobank:
   • Discuss project with Director/Manager
   • Pathologist
Clinical Data

- Annotation and uniform terminology
  - caBIG – common data elements
  - caTissue Suite
- Informatics support
- Participant authorization, privacy, human subject regulations
- Process for confirming and validating clinical data
- Track requests
- Longitudinal data management
Tumour Banking in Canada

CTRNet:

- Not-for-profit consortium – CIHR funding
- Virtual bank linking provincial tumour banks
- Single electronic portal of access
- Promoting administrative and scientific best practice
  - Marble Arch Consortium – international group developing standardized SOPs
Biobanking and NCI

- 2002 – surveys and community forums
- 2003 – National Biospecimen Network Blueprint
  – Case Studies of Existing Human Tissue Repositories
- 2004 – Office of Biorepositories and Biospecimen Research (OBBR) – Carolyn Compton
- 2007 – NCI Best Practices for Biospecimen Resources
- 2007 – Workshop on Custodianship and Ownership Issues in Research Using Biospecimens
- 2008 – OBBR – Advancing Cancer Research Through Biospecimen Science
Biobank Informatics

- Interoperability
- Secure, monitored
- Flexibility
- Networking capabilities
- System qc
- Adherence to established ethical legal policy
Cancer Centres – IT*

- **Integrated Systems**
  - Homegrown/Commercial
  - Smooth navigation between applications
  - Difficult to expand/extend
  - Large IT staff
  - $10M’s invested

- **Heterogeneous Systems**
  - Complex mix of commercial and homegrown components (may be composed of dozens of components)
  - No common interfaces
  - Medium size IT staff
  - $1M’s invested

- **Informal/no systems**
  - Use of productivity applications (e.g. Excel, Access)
  - Complex manual processes
  - Small or no IT staff
  - $100K’s invested

* Adapted from Ken Buetow, Ph.D. NCI Associate Director Bioinformatics and Information Technology
PMH/UHN BioBank

- Dept of Pathology
  - manages UHN resource
  - 38 sub-specialty pathologists
  - Synoptic Reporting (CAP)
  - disease specific banking protocols
- PMH Cancer Registry
PMH/UHN BioBank: Cases Per Year

- 2001: 900 cases
- 2002: 1500 cases
- 2003: 1700 cases
- 2004: 1900 cases
- 2005: 2300 cases
- 2006: 1800 cases
- 2007: 2600 cases
BioBank Core Laboratory

- **Storage / Retrieval**
  - Tissue
  - Effusions
  - Paraffin Block Bank

- **Processing**
  - Tissue Microarray Facility
  - Laser Capture Microdissection
  - RNA/DNA/Prot.

- **Digital Image Library**
  - Quality control
  - Tissue content
  - Annotation for TMA

- **Standardized Blood Collections**
  - Pre-op

DIAGRAM:
- Blood
- Snap Frozen
- Fluids
- Paraffin Blocks/Slides
- TMAs
- Live Cells
- Digital Image Library
- 13,970

Connections:
- Blood → Snap Frozen
- Snap Frozen → Fluids
- Fluids → Paraffin Blocks/Slides
- Paraffin Blocks/Slides → TMAs
- TMAs → Live Cells
- Live Cells → Digital Image Library
- Digital Image Library → 13,970
- 13,970 → Blood