Biobanking: The Past, Present, and Future

Medical Oncology CE

Sept 19, 2008

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Dept. of Pathology

Toronto Ovarian Tissue Bank and Database

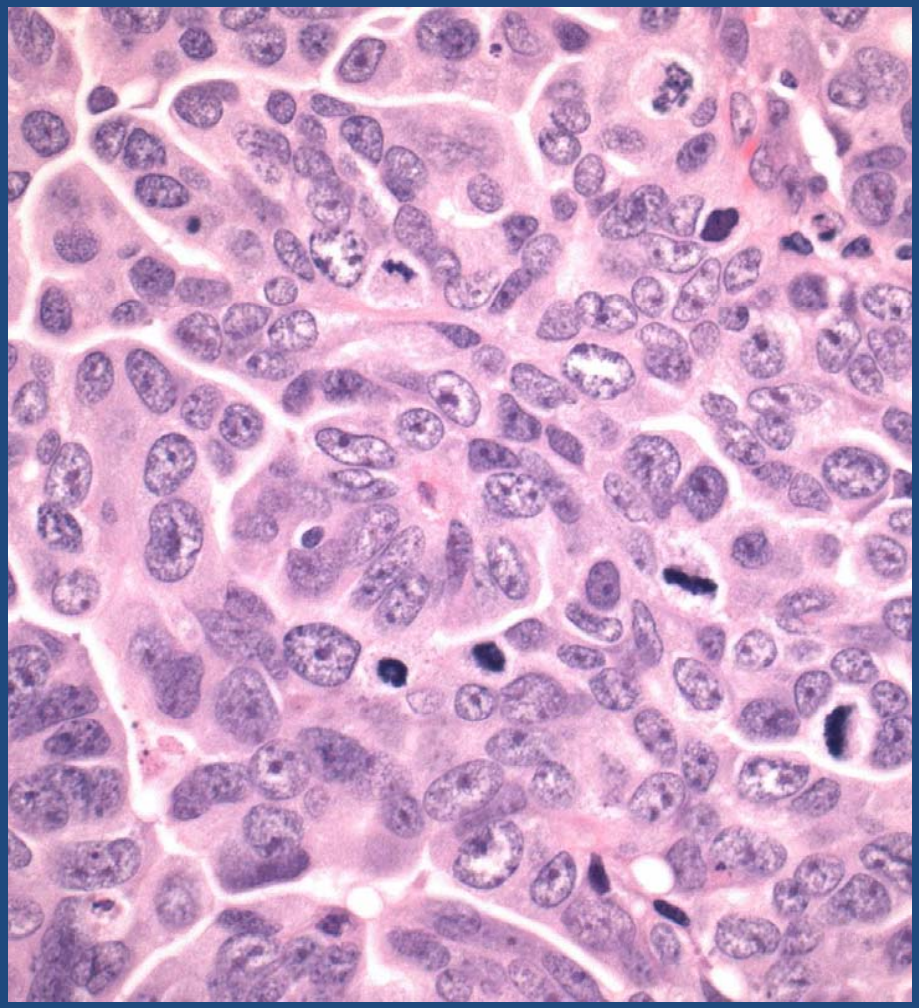
- Samples:
  - Snap frozen tissue
  - normal
  - benign
  - LMP
  - Malignant, primary and metastatic
- Paraffin blocks and glass slides
- Ascites
- Blood
- Comprehensive database - Pathology, clinical, family history, treatment, follow up

STAGE AND HISTOLOGICAL TYPE*

	Stage I-II	Stage III-IV	Total (n)
Endometrioid	84%	16%	9%
Mucinous	77%	23%	6%
Clear cell	53%	47%	9%
Serous	*6%*	*94%*	*75%*
HGSCa	*<2%*		
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

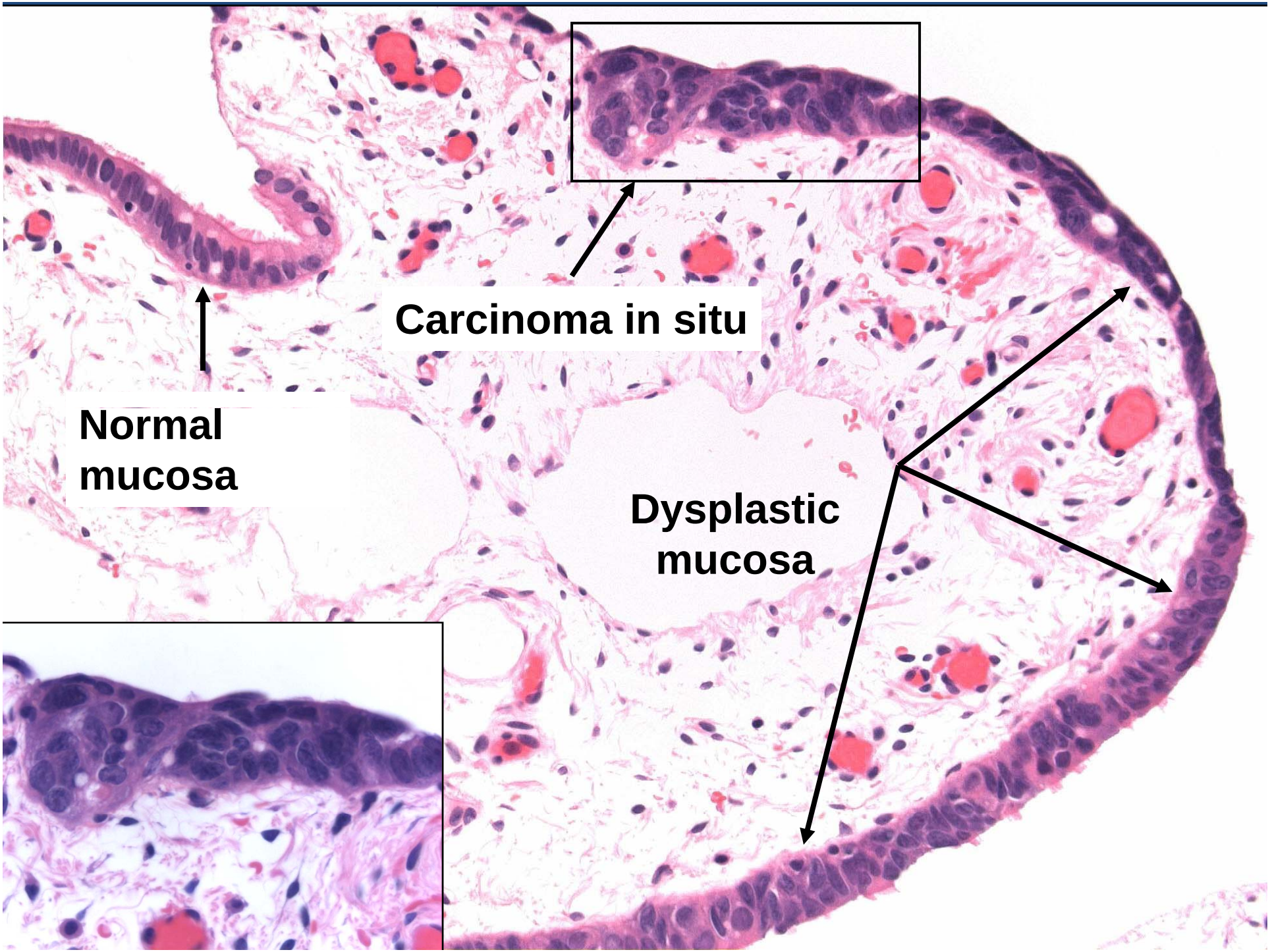
Shaw et al 2002

OCCULT CANCERS IN PROPHYLACTIC SALPINGO-OOPHORECTOMY SPECIMENS

159 patients:

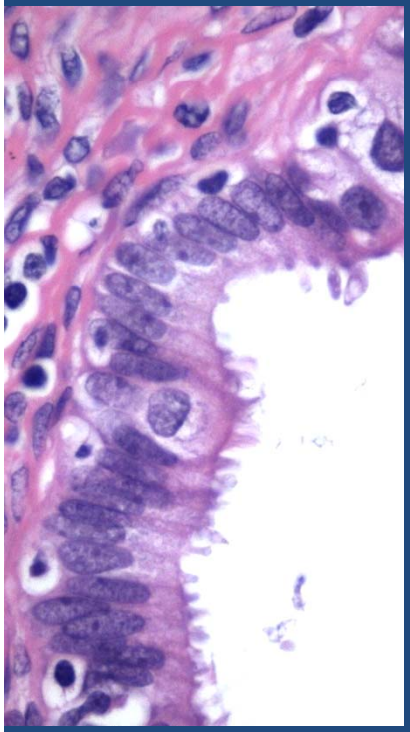
	BRCA1 (94)	BRCA2 (64)
Cancer diagnosis at surgery	6 (6.4%)	1 (1.6%)
Mean age at diagnosis	49.5 yr.	53 yr.
Cancer Type	Serous grade 3	Serous grade 3
Cancer site	5/6 tube 3/6 ovary & tube 1/6 ovary only	Peritoneum

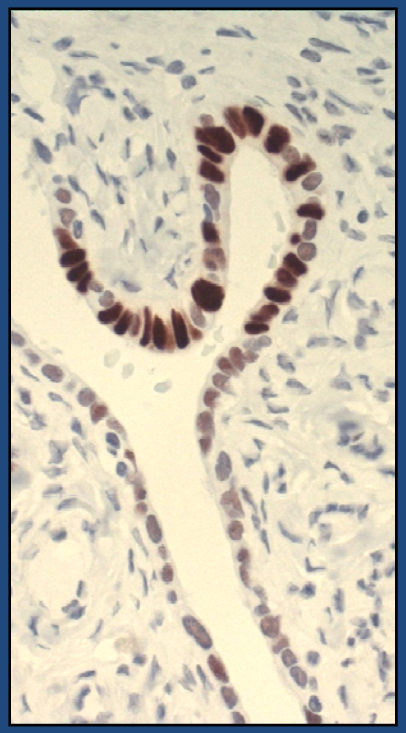
Finch et al 2006

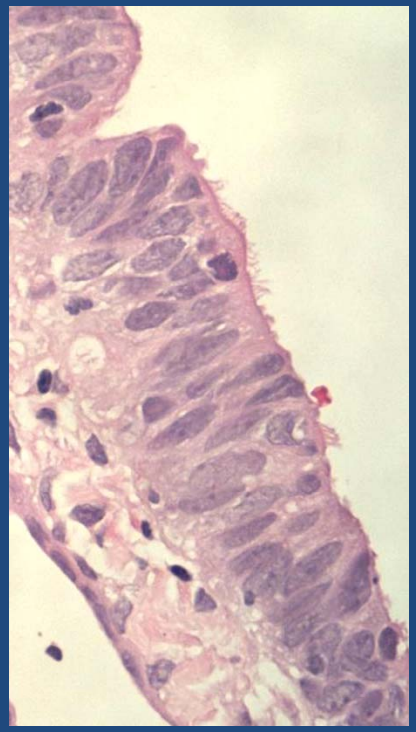

Carcinoma in situ
Normal mucosa
Dysplastic mucosa

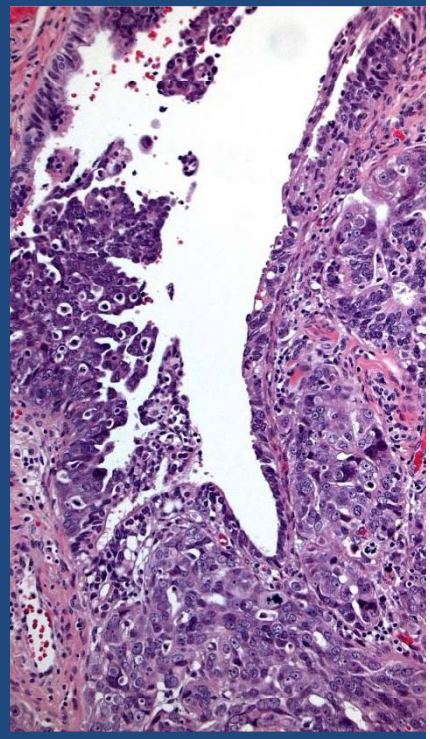
A New Model for High Grade Serous Tumorigenesis

Normal → p53 Signature → TIC → HGSCa

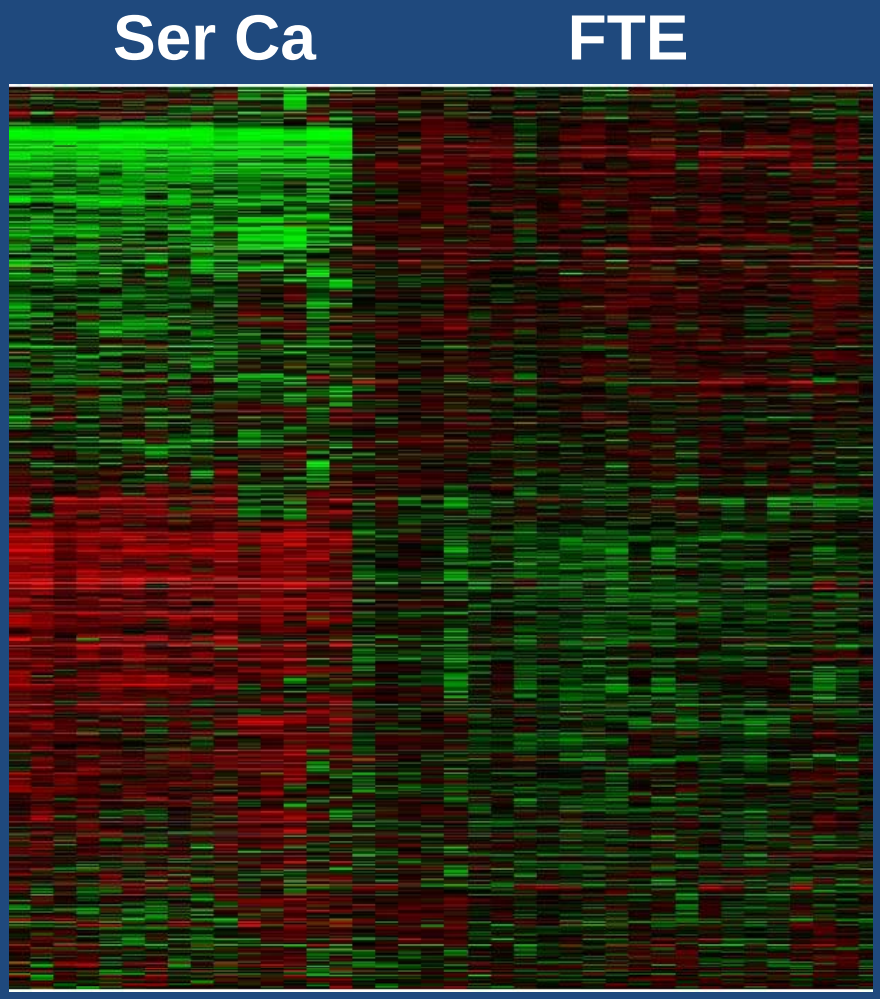








BRCA1

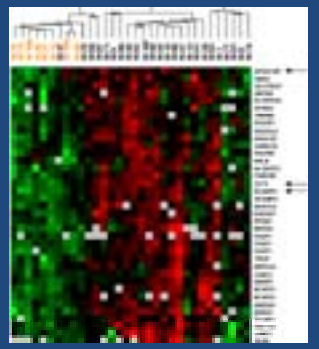


Gene Expression Profiles of Luteal Phase Fallopian Tube Epithelium from *BRCA*-Mutation Carriers Resemble High Grade Serous Carcinoma

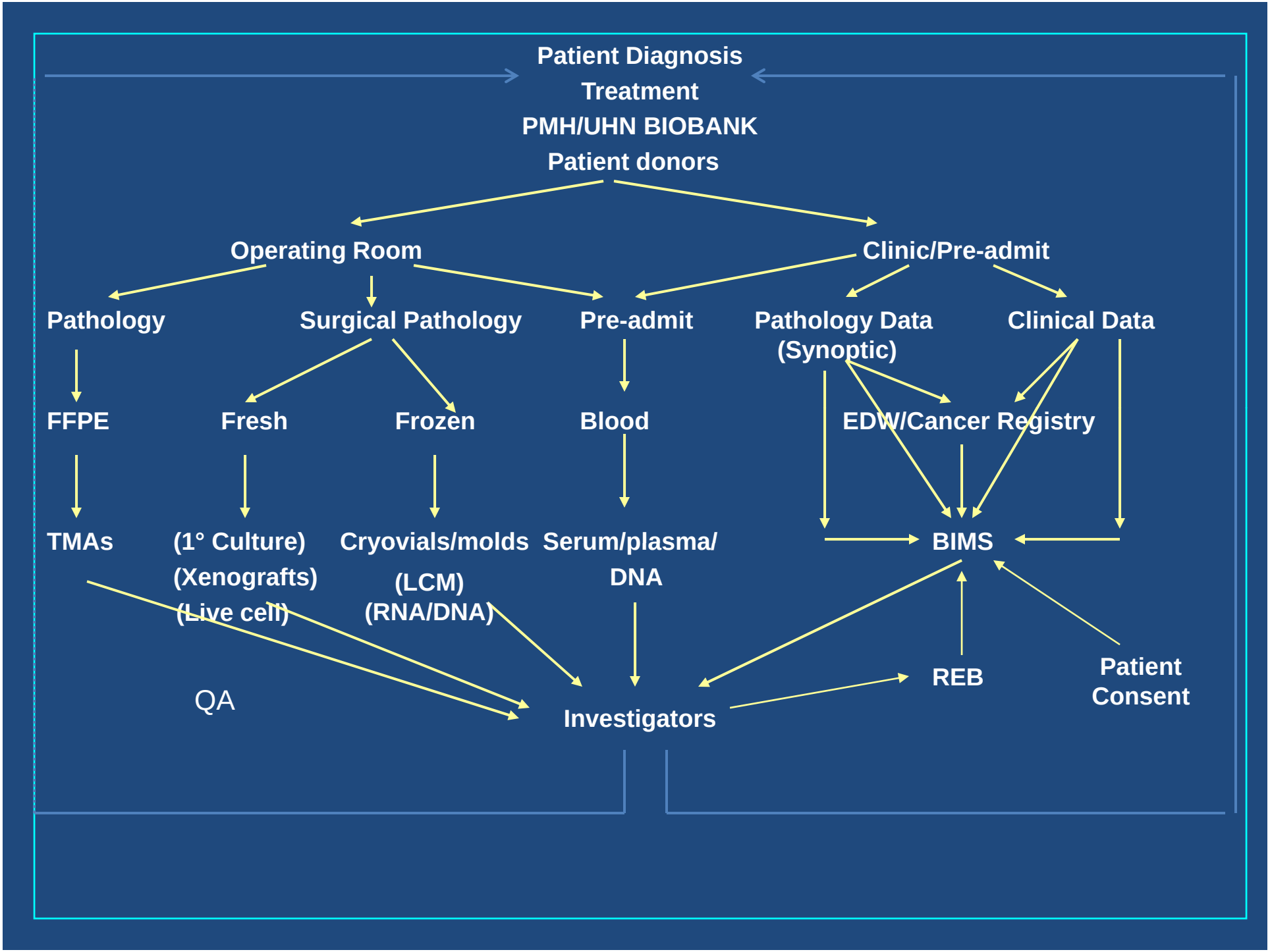
Tone et al CCR 2008

Patient/Clinic

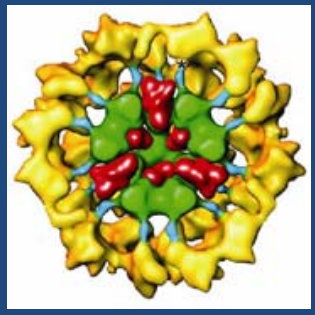
Discovery



Biobank


Patient Diagnosis
Treatment
PMH/UHN BIOBANK
Patient donors
Operating Room
Clinic/Pre-admit
Pathology
Surgical Pathology
Pre-admit
Pathology Data (Synoptic)
Clinical Data
FFPE
Fresh
Frozen
Blood
EDW/Cancer Registry
TMAs
(1° Culture) (Xenografts) (Live cell)
Cryovials/molds (LCM) (RNA/DNA)
Serum/plasma/ DNA
BIMS
QA
Investigators
REB
Patient Consent

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

Patient Procedure Collection Processing Storage Distribution Analysis

- Anesthesia
- Drugs
- Clamp time

Time 0

- Type of tube
- Time at room temperature
- Rate of freezing
- Time in fixative
- Size of aliquots

Pre-analytical Variables

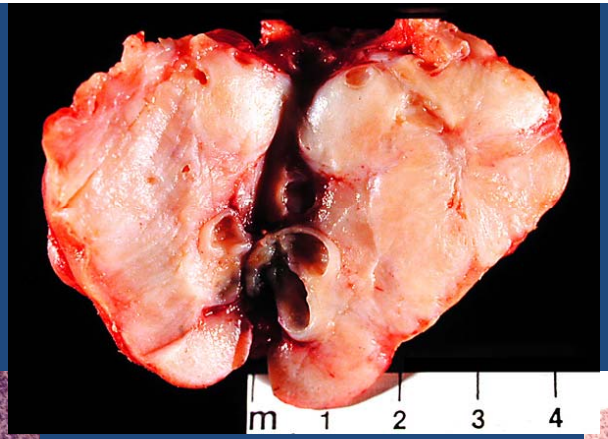
Quality of sample handling:

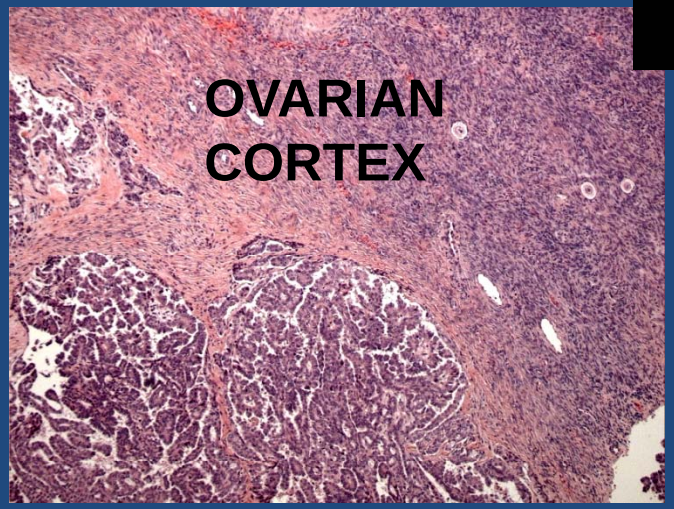
- **Her2-neu IHC**
  - **Very specific instructions for use to get validated results:**
    - **Thickness of section**
    - **Formalin minimum & maximum**
    - **Ag retrieval and buffer**
- **in community there is a high false positive rate and a 20% false negative rate**
- **FISH (Pathvision)– if 2+ - FISH will be false negative if fixed over weekend**

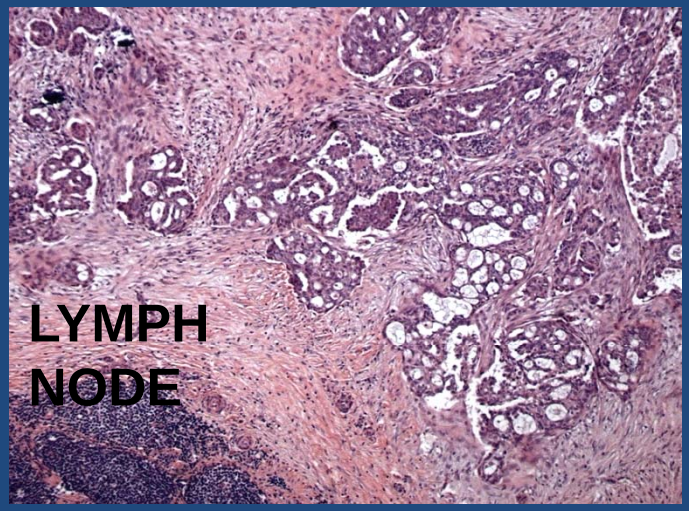
Effects of tissue processing techniques on biomarker analysis :

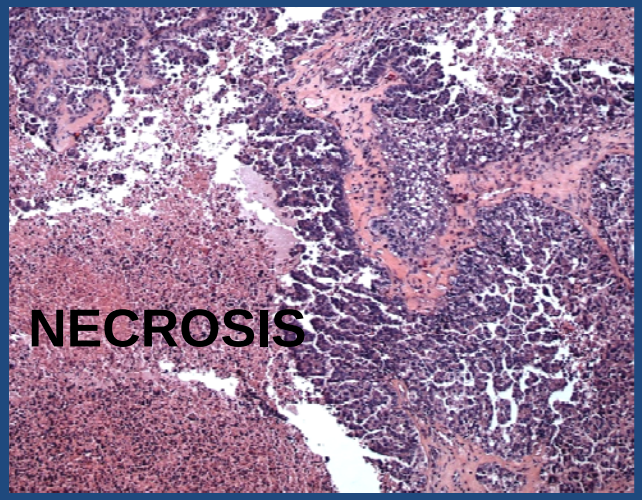
- time of post-fixation
- temp of paraffin
- section thickness,
- water bath temp
- ? ammonia
- time and temp of slide drying
- ? Baking
- ? Deparaffinize
- how to store

Tumor Content









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


What's a biobank?
What am I agreeing to?
Perhaps you'd like to donate some of your genes to a biobank

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

   banking protocols
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*

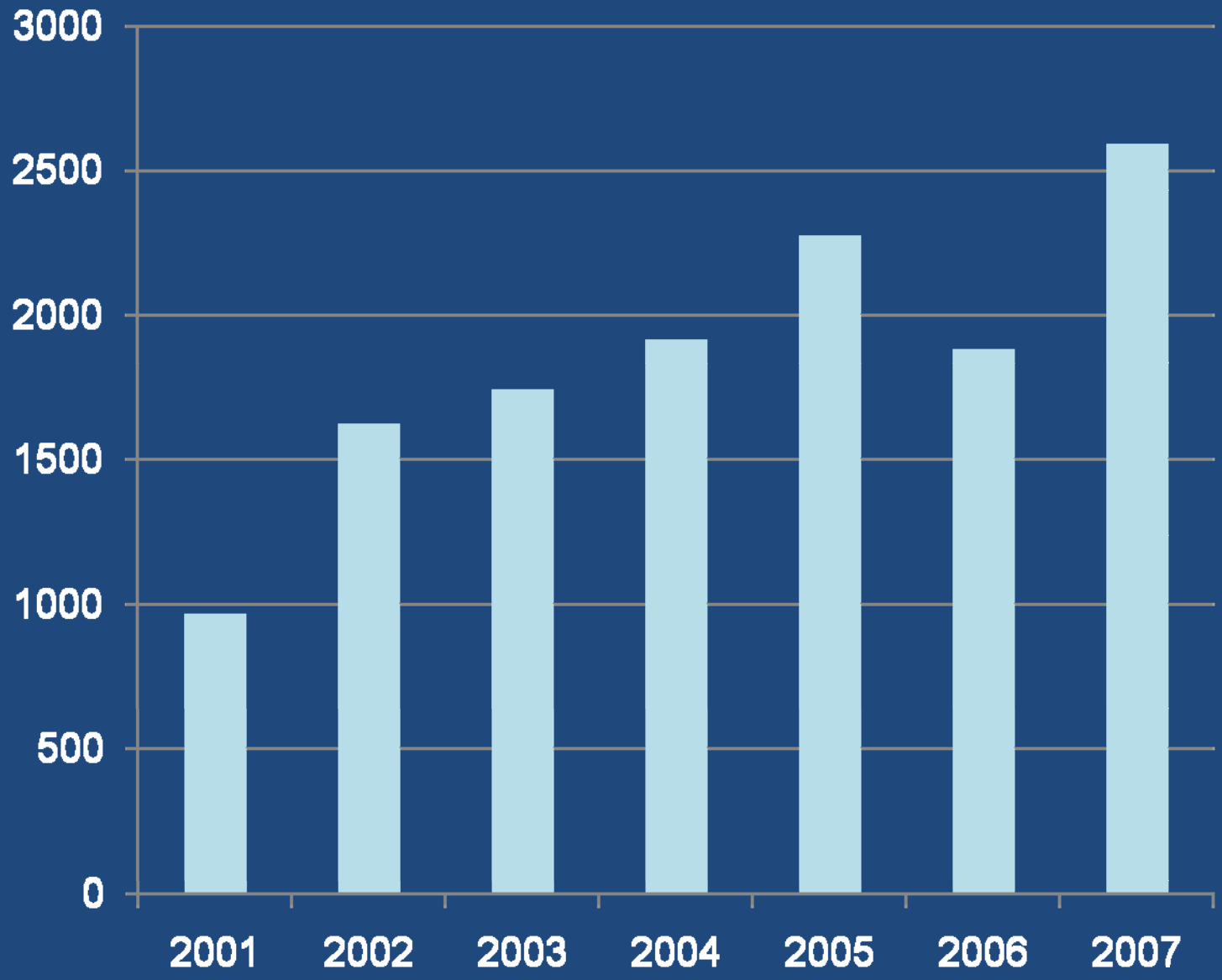
- Integrated Systems
  - Homegrown/ Commercial
  - Smooth navigation between applications
  - Difficult to expand/extend
  - Large IT staff
  - $10M's invested
- Heterogeneous Systems
  - Complex mix of commercial and homegrown components (may be composed of dozens of components)
  - No common interfaces
  - 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

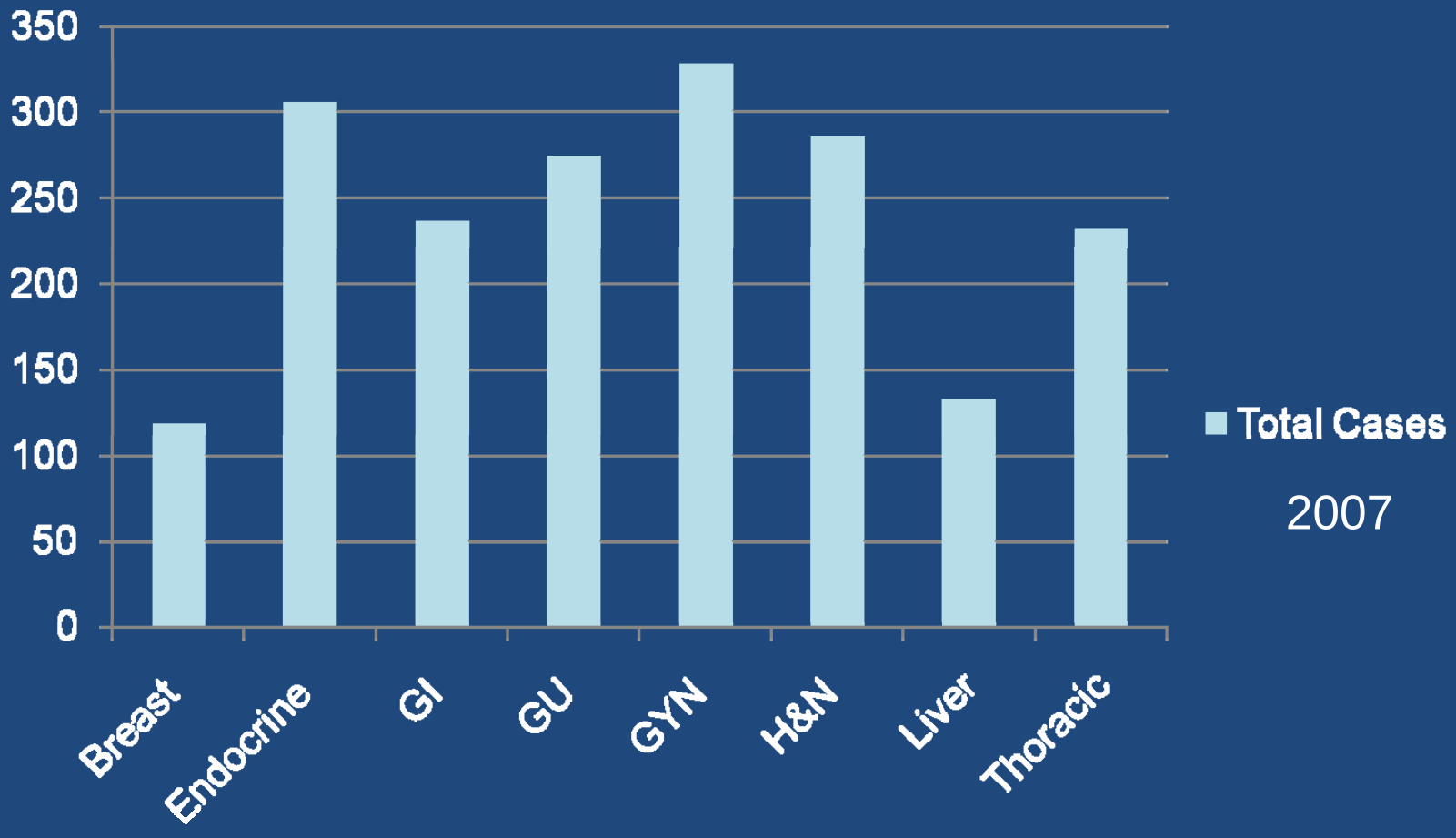
PMH/UHN BioBank

- 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

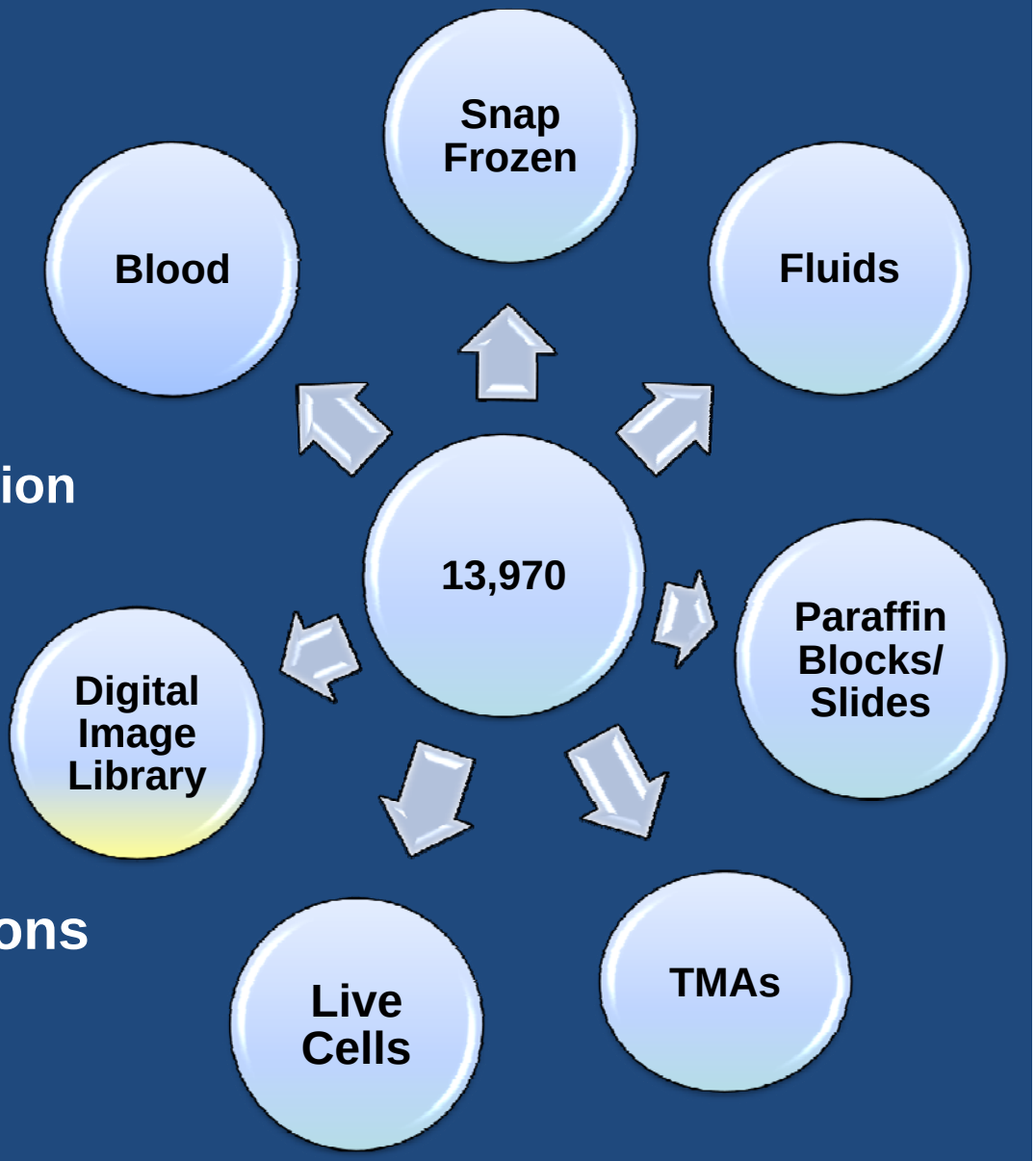


PMH/UHN BioBank: Donors By Disease Site

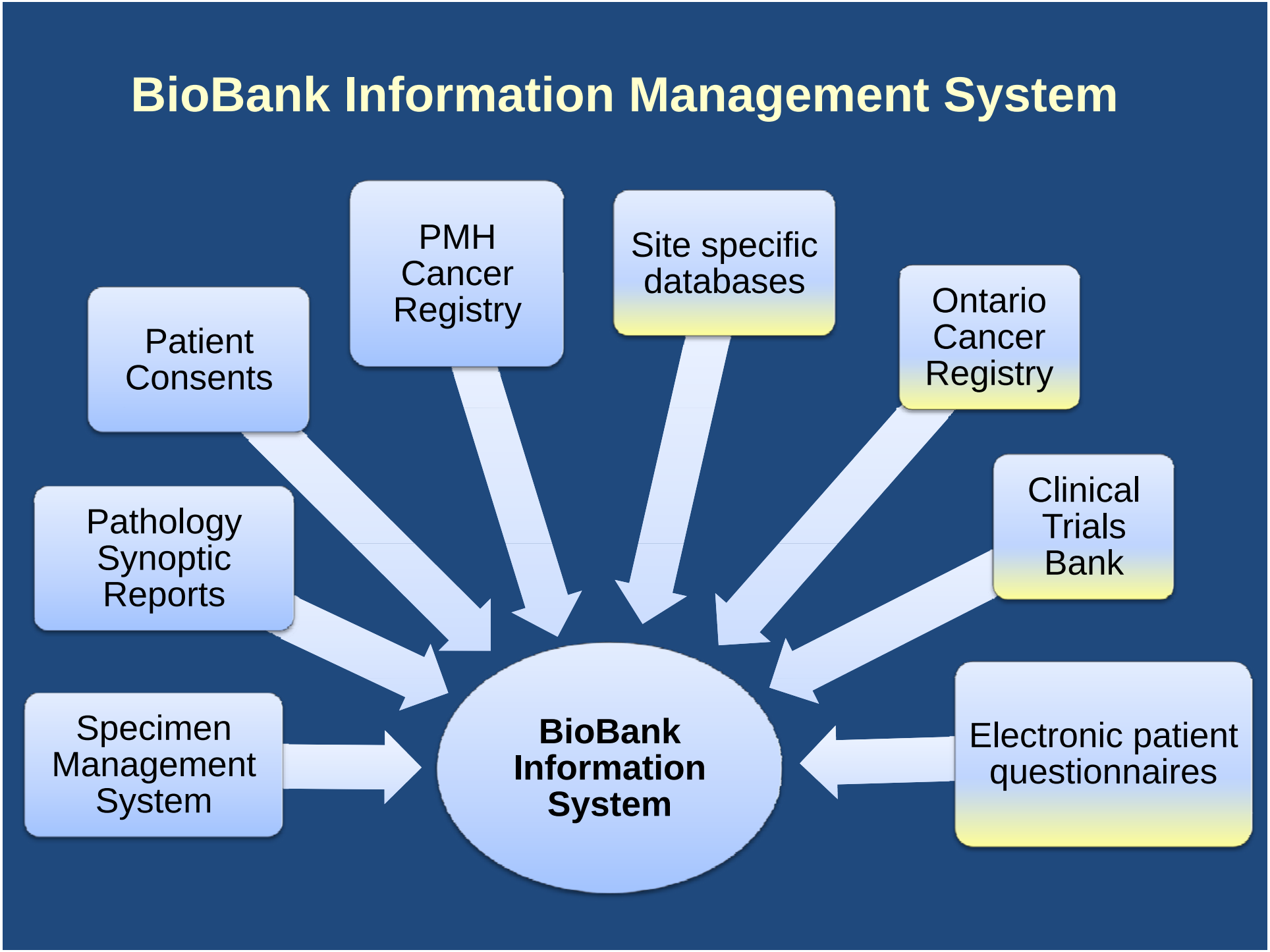


BioBank Core Laboratory

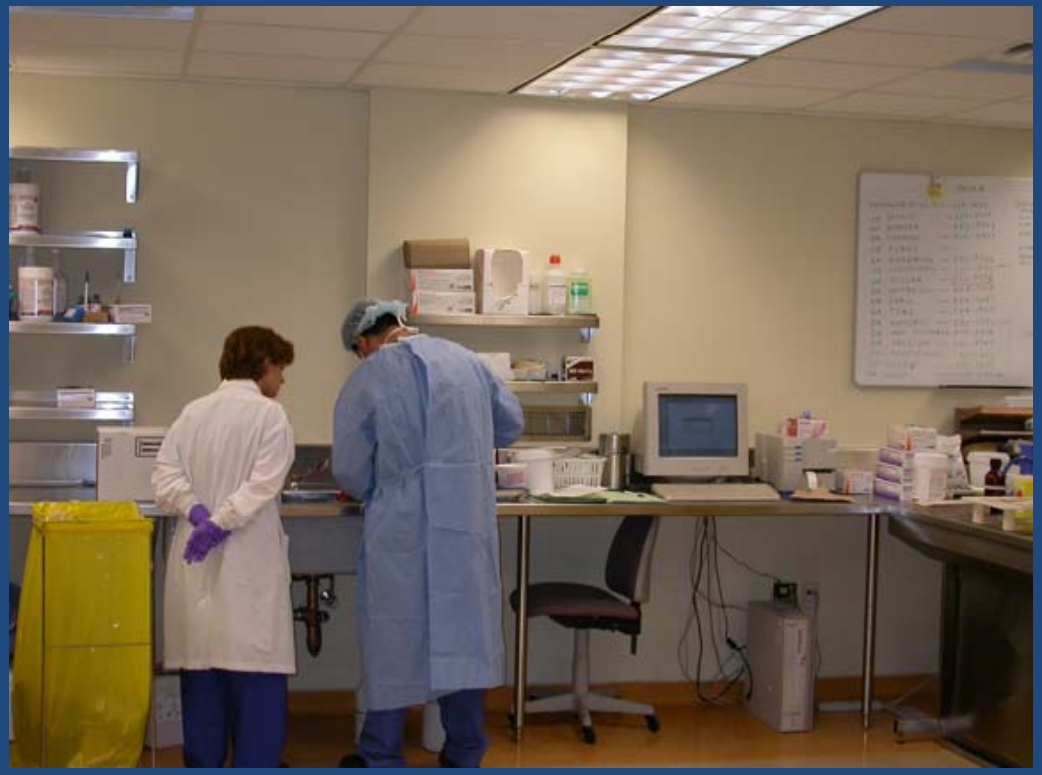
- **Storage / Retrieval**
  - Tissue
  - Effusions
  - Paraffin Block Bank
- **Processing**
  - Tissue Microarray Facility
  - Laser Capture Microdissection
  - RNA/DNA/Prot.
- **Digital Image Library**
  - quality control
  - tissue content
  - annotation for TMA
- **Standardized Blood Collections**
  - Pre-op



BioBank Information Management System



PMH/UHN BioBank



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