Biobanking in the UC System: Creating uniform, high-quality standards to benefit research and clinical care

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What is Biobanking?

- Collection, storage and distribution of human tissues or fluids (blood, urine, etc.) for research
- Remnant diagnostic samples
- Targeted prospective research collections
- “Secondary use” samples
- Clinical data adds value
Why Biobanking?

- Essential for translational research, including drug development (targeted therapies)
- Often mandatory for clinical trials
- Required for Personalized Medicine
- Valuable for health informatics
  - Medication compliance in populations
  - Monitoring physician/hospital compliance with practice recommendations
Anyone could/did keep samples in freezers
Informed consent not routine until 1980s
S/he who has it, owns it
OR cases received in Pathology with large pieces of tumor missing
Standard Operating Practices (SOPs) rare
No acceptable measures of quality
All samples considered equally good – no understanding of effect of warm ischemia, transport media, etc
All biobanks are high quality, right?

- The Cancer Genome Atlas experience
  - 2006 NIH Office of Biorepositories and Biospecimen Research (OBBR) publically requested samples of 3 tumors: brain (GBM), lung (SCC) and ovarian (serous papillary) as pilot project
  - “Acceptable” sample parameters (size, percent tumor, percent necrosis) predefined by experts
  - Goal = 500 samples per tumor
  - Large response; OBBR felt all 1,500 samples required could be collected from 4–6 institutions
Reality of TCGA experience – GBM

- Used GBM samples already stored in freezers
- Drop out rate approached 99%
  - Samples on hand did NOT match what biobanks thought they had (tumor, matched normal, size)
- Submitted samples
  - 40% failed histology requirements
  - Further 25% failed molecular quality testing
- Required expansion to 54 institutions and addition of prospective collections for subsequent tumors
- Published GBM (2008, n=143), ovarian (2011, n=489), lung (2012, n=178)
  - Ovarian: 20% fail histology reqs, 24% fail molecular QC
  - Lung: 17% fail histology, ?0% fail molecular QC
Standardizing biobanking operations

- 2002 International Society for Biological and Environmental Repositories (ISBER)
  - Under American Society for Investigative Pathology
  - Journal, Annual Meetings, website, litserv

- 2005 NIH OBRR
  - Annual Meetings
  - Website with data, other information

- 2011 College of American Pathologists (CAP) Biorepository Accreditation Program
Emerging into the spotlight...

- 2007 Catalona vs. Wash Univ
  - Universities, NOT individual researchers, owners of research biorepository collections

- Informed consent
  - On-going debate over last decade
  - 2011 Proposed changes to the Federal Human Subjects Research Protections
  - 2012 Senate bill (Padilla)

- NIH RFA May 2012 for informed consent and biobanking
Popular Press Highlights Issue

The Immortal Life of Henrietta Lacks

Doctors took her cells without asking. Those cells never died. They launched a medical revolution and a multimillion-dollar industry. More than twenty years later, her children found out. Their lives would never be the same.

Rebecca Skloot
An institutional resource?

- New institutional biobanks
  - MDACC, Partners
    - MDACC has clinical biobank for personalized medicine in addition to research biobank
  - Individual collections continue to exist, but not clear how long this will be viable

- Substantial institutional investments
  - Partners $10 million
UC BRAID Biobanking Working Group

- UCLA: Sarah Dry (Chair), Steve Dubinett
- UC Davis: Josh Miller, Yvonne Wan
- UC Irvine: Dan Mercola
- UC San Diego: David Boyle
- UC San Francisco: Julie Auger, Britt–Marie Ljung, Hubert Stoppler, Margaret Tempero
- Administrative support: Courtney McFall

- Is UC now able to derive maximal benefit from its existing biobanks?
Current State of UC Biobanking

- Similar to all academic centers nationally:
  - Each UC campus has many separate biobanks, each approved by campus IRB = million samples possible
  - Each biobank runs by its own rules
  - No standard set of recommended or “best” practices
  - No central registration for biobanks (other than IRB)
  - Most collections private and secret

- Difficult to identify and access samples if not part of the collecting group

- Currently any freezer/refrigerator with human samples for research = biobank
“UC–recognized” Biobanks will adopt standardized operating procedures, quality control measures and staff training appropriate to their specific biosample collections so that:

- The biobank conforms to NIH, CAP, ISBER standards
- The biosamples are of the highest possible quality
- The biobanks meet the ethical operating standards of all campus IRBs

Meeting the above will enable:

- Multi-campus research (biomedical, health informatics)
- Higher researcher confidence in sample quality
- Easier and more rapid biobank accreditation
- Conformation with higher quality biosample standards that are already affecting grant scores and paper reviews
“Integrated biobanking with uniform, high-quality standards, is required to provide the biosamples critical to the success of UC research and clinical care at all 5 campuses”

- Short-term goal: Develop standards for “UC recognized” biobanks
- Medium-term goal: Help interested UC banks achieve standards to be “UC-recognized”
- Ultimate goal: create a network of high-quality “UC-recognized” biobanks that are willing to share samples across UC system
Uniform Biobanking Amplifies Benefits of other BRAID Efforts

- Cohort finding (UC Rex)
  - Bi-directional benefit
- Drug Discovery and Development
- Harmonized IRB
- Master Contracting
Areas to be addressed

- **Operations**
  - Practical functioning of the biobanks
  - Entire biosample lifetime, from pre-procurement through distribution/destruction
  - Established “Best Practices” recommendations from 3 national/international groups available
  - Amenable to standardization

- **Governance**
  - Control of samples: who may receive, criteria to receive, how to allocate rare/precious samples, who reviews/determines, appeals process?
  - Unique institutional or programmatic exigencies could make standardization a challenge
Establish recommended Standard Operating Procedures (SOPs) for biobanks, including:
- Specimen handling (procurement, storage, distrib)
- Specimen processing (DNA/RNA)
- Storage systems (temperature monitoring, alarms)
- Database/IT
- Informed consent/IRB
- Quality Assurance/Quality Control program

Develop model SOPs that banks can edit to meet their specific needs
Our Challenges – Operations

- Biosample type and intended use vary greatly
- Recommended SOPs must be written to ensure biobanks address critical factors associated with quality, without:
  - Interfering with necessary quality operations
  - Undue burden (financial, time, other) on banks

- Informed Consent
  - Absence of standardized IC practices and lack of standard IRB expectations for biobanks will limit ability to exchange samples between campuses
Informed consent challenge

- Current practices range from no consent to full informed consent, within all campuses
- Certain collections (ie, clinical trials) uniformly have IC throughout all campuses
- Remnant diagnostic sample biobanks
  - Most variation in current practices within UC
  - Have largest barriers to implementing IC
- If funded, the EngageUC grant addresses this as a main aim, and will include involvement of campus Institutional Officials, patient communities, biobanks and researchers
Accomplishments to date

- Submitted NIH grant (EngageUC) for informed consent and biorepositories (Dry – Co-Program Director, all UC biobanking working group members as collaborators)
- First formal meeting as BRAID working group in mid–July 2012
- Agreement on vision, goals, achievable changes and challenges
- Finalized survey language on current biofluid and tissue collection/storage practices
- Developing SOP recommendations for tissues/fluids procurement (anticipated final by mid–October)
Goals – next 12 months

- Finalize SOPs for all Operations areas
- Determine best method to assist biobanks to achieve “UC–recognized” biobank standards
  - Educational component
  - May involve a pilot project
- Address governance recommendations
- Discuss governance issues for sample sharing across UC Regional Research Network
- If funded, work to meet aims of “UC Engage”