Ethics of Biobanking

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PRE-CONFERENCE PROGRAM

Contemporary Issues in Biobanking: Governance, Consent, and Practical Approaches to Current Challenges

Biobanking: Definition

- "Biobank" first appeared in scientific literature in 1996.
- What is a Biobank?
- 303 survey responses from managers of sample collections
- There is consensus that the term biobank may be applied to biological collections of human, animal, plant or microbial samples; and that the term biobank should only be applied to sample collections with associated sample data, and to collections that are managed according to professional standards.
- There was no consensus on whether a collection's purpose, size or level of access should determine whether it is called a biobank.

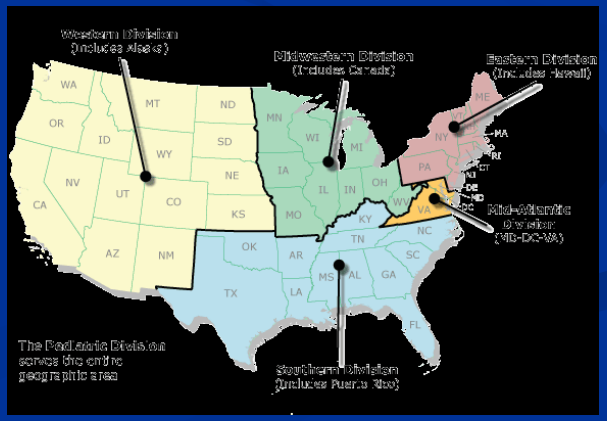
Hewitt R, and Watson P . Biopreservation and Biobanking. 2013, 11(5): 309-315

Biobank: Examples

- Small, Disease Specific Collections

- Cooperative Federal Projects Prospectively Collecting Samples

CHTN
COOPERATIVE
HUMAN TISSUE
NETWORK



- Established in 1987 via NCI Support
- Funded Through March 31, 2019
- Goal: Provide biomedical researchers with wide variety of high quality, well characterized human tissues to support cancer research
- ***Credit for success measured not by banking but by specimens distributed to researchers.***

Biobanking: Scope

- > 300 million tissue samples in US Banks at turn of the century.
- Samples increasing by 20 million/yr
  Eiseman, E. & Haga, S. *Handbook of Human Tissue Sources* (RAND, 1999).
- A 2011 survey of >700 cancer researchers found that 47% had trouble finding samples of sufficient quality, and must limit scope of investigation. Massett, H. A. *et al. J. Natl Cancer Inst. Monogr.* **2011**, 8–15 (2011).

Biobanking Benefits

- Stored samples will be used for the development of products and services that promote public health.
- Fosters cross-collaboration between disease advocacy organizations and research scientists.
- Biobanking produces synergy that hastens the research process.

Ethical Challenges/Controversies

- Informed Consent
- Confidentiality; Breach of Privacy
  - Genetic Discrimination
    - Finance, Insurance, Employment
- Ownership and Commercialization

Ethical Challenges/Controversies

- ***Informed Consent***
- Confidentiality; Breach of Privacy
- Financial Discrimination
- Ownership and Commercialization

Elements of Informed Consent: CFR 46.116

1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

Is this possible.????

Elements of Informed Consent: CFR 46.11

- Biobanks are not research projects, but rather a resource for many projects.
- Biobanking is "future oriented." *Purpose, length of participation, procedures* change.
- Biobank consent may involve other individuals besides research subject.

Widdows H, Cordell S (2011). The ethics of biobanking: key issues and controversies. Health Care Analysis, 19 (3) 207-219

Elements of Informed Consent: CFR 46.11

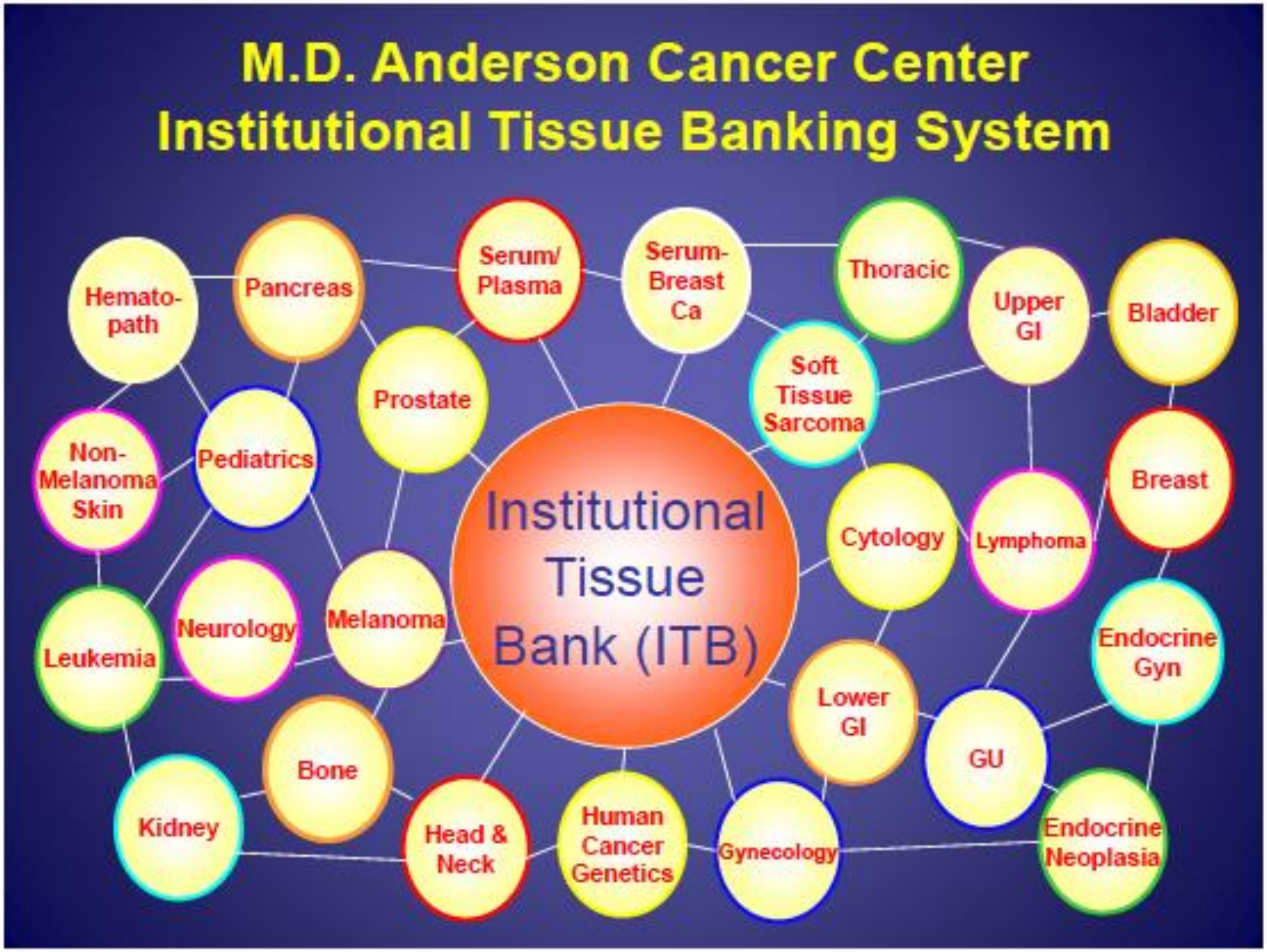
- Connected Individuals: Those not directly involved in the study whose health might be directly affected by genetic results
  - ***Huntington's Disease***
  - ***BRCA1 or BRCA2***
- May affect family or larger community

Widdows H, Cordell S (2011). The ethics of biobanking: key issues and controversies. Health Care Analysis, 19 (3) 207-219

Elements of Informed Consent: CFR 46.11

- A statement that …the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Is this possible????


M.D. Anderson Cancer Center
Institutional Tissue Banking System
Institutional Tissue Bank (ITB)
Hemato-path
Pancreas
Serum/ Plasma
Serum-Breast Ca
Thoracic
Upper GI
Bladder
Prostate
Soft Tissue Sarcoma
Non-Melanoma Skin
Pediatrics
Breast
Cytology
Lymphoma
Leukemia
Neurology
Melanoma
Endocrine Gyn
Lower GI
GU
Bone
Kidney
Head & Neck
Human Cancer Genetics
Gynecology
Endocrine Neoplasia

Informed Consent: Belmont Report

- Respect for persons requires that subjects, to the degree that they are capable be given the opportunity to choose what shall or shall not happen to them.

Informed Consent Models

- Opt-In
- Opt-Out
- Disease/Study Specific
- Tiered Consent
- Broad Consent
- Dynamic Consent

Informed Consent Models

- ***Opt-In***
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DANA-FARBER
CANCER INSTITUTE

BRIGHAM AND
WOMEN'S HOSPITAL

Cancer Research Study

Researchers at Dana-Farber Cancer Institute (DFCI) and Brigham & Women's Hospital (BWH) want to learn as much as possible about the causes of cancers and leukemias and to find new ways to treat them.

1. What is a research study?

A research study is an effort to learn more about a problem or to answer questions.

2. What is the purpose of this study?

Its purpose is to analyze some of your tissues and fluids and link that information with your clinical health information.

3. Why am I being asked to participate?

You are being asked to participate because:

- You have or have had cancer; or
- You are thought to have an increased risk for cancer

4. Do I have to participate in this study?

No. Taking part in this study is voluntary. Your care at DFCI or BWH will not be affected if you choose not to participate. Even if you decide to participate, you can change your mind and leave the study at any time. If you choose not to participate, or decide to participate and then later withdraw, you will not suffer any penalty or lose any benefits to which you are otherwise entitled.

5. Will I benefit from participating?

While taking part in this study may not improve your own health, we hope that the information we collect will aid in our research efforts to provide better cancer treatment and prevention options to future patients.

6. Will I learn the results of this study?

In general, we do not plan to contact you about the results of this study. However, a small number of the analyses we perform may have clinical importance. For example, they might uncover characteristics known to make cancers responsive to specific therapies. In addition, some of the analyses that currently have no clinical importance may later be discovered to have some.

Informed Consent Models

- Opt-In
- ***Opt-Out***
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- Broad Consent
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Opt-Out: Vanderbilt

- 45 CFR 46.102 (f), defines a "Human Subject" as a living individual about whom an investigator conducting research obtains either data through intervention or interaction with the individual, or identifiable private information, or an individual who is or becomes a participant in research.

- BioVU accrues DNA samples extracted from discarded blood samples scheduled to be discarded. (No interaction)
- The resource is linked to a de-identified version of data extracted from an Electronic Medical Record (EMR) system, called the Synthetic Derivative (SD), in which all personal identifiers have been removed. (No identifiable PHI)

De-Identified Samples:

- Names
- Geo. Subdiv.<State
- Date (Except Year)
- Telephone #
- Fax #
- Email
- SSN
- Medical Rec. #
- Health Plan Benefic.#
- Account #
- Certificate/License #
- Vehicle Identifiers
- Device Identifiers
- URLs
- IP #
- Biometric Identifiers
- Full Face Photo
- Any Other Identifier

Perceived Harm from Biobank Research

- ***Beleno et al v Texas Dept. of State Health Services***
- Bloodspots from newborns biobanked for genetic research w/o parental consent
- State agreed to destroy > 4 million blood samples and disclose financial transactions.

Perceived Harm from Biobank Research

- ***Havasupi Tribe v Arizona State University Board of Regents***
- Consent provided for study of diabetes from genetic samples.
- Studied, without consent, schizophrenia, ETOH, inbreeding
- Havasupai compensatedd $700K.
- All samples, all data returned.

Vanderbilt: Opt In

- **BioVU Research Form**
- When your doctor orders blood tests, there is usually some blood left over after the tests are done. In the past, this blood was thrown away. BioVU is now saving this extra blood for research. We will save your blood if you sign the BioVU Research Consent Form. If you don't want to participate in BioVU, do not sign the form.

Informed Consent: Genomic Research NIH

- http://gds.nih.gov/03policy2.html
- Jan. 2015: Designed to promote robust sharing of data from a wide range of genomic research and to provide appropriate protections for research involving human data.

Informed Consent: Genomic Research NIH

- http://gds.nih.gov/03policy2.html
- Two fundamental components of informed consent:
  - ***a dialogue or process***
  - ***a form***

Informed Consent Models

- Opt-In
- Opt-Out
- ***Disease/Study Specific***
- Tiered Consent
- Broad Consent
- Dynamic Consent

Disease/Study Specific Consent

- Cancer, Heart Disease, ID, etc.
- Encourages participant involvement
- Restricts downstream usage of samples
- Who determines appropriateness of sample distribution??

Informed Consent Models

- Opt-In
- Opt-Out
- Disease/Study Specific
- ***Tiered Consent***
- Broad Consent
- Dynamic Consent

Tiered Consent

- Research subject picks and chooses among research projects/diseases
- Requires rigorous (*expensive*) tracking over time to make sure subjects' wishes are followed
- "One from Column A……"

Tiered Consent

Soup

G.S.T. Included

Long Soup (Egg Noodle) $5.20
Short Soup (Won Ton) $5.20
Combination Soup $5.20
(mixed vegetables, chicken & pork)
Chicken & Sweet Corn Soup $5.20
Prawn & Sweet Corn Soup $5.20
Crab Meat & Sweet Corn Soup $5.20

Appetizers & Entree

Vegetarian Mini Spring Rolls (4) $4.80
Mini Spring Rolls (4) $4.80
Home Made Dim Sims
(Steamed Or Fried) (4) $4.80
Tasty Deep Fried Chicken Wings $4.80
Sesame Prawn Toast $5.20
King Prawn Cutlets (3) $6.60
Mixes Entree $5.20
(Spring Roll, Fried Dim Sim & King Prawn Cutlet)
Prawn Cocktail $6.90
Garlic King Prawns $10.00
Prawn Chips $2.80

Main Meal

First select a sauce option then select a meat option

Satay Sauce
Szechuan Sauce
Plum Sauce
(onion , celery, carrot, capsicum, baby corn and mushrooms)
Black Bean Sauce
Barbeque Sauce
(broccoli, onion, celery, carrot, capsicum, baby corn and mushrooms)

Main Meal (Continued)

Oyster Sauce
Garlic Sauce
(broccoli, onion, celery ,carrot, baby corn and mushrooms)
Chilli Sauce
(broccoli, onion, celery, carrot, baby corn, mushrooms ,capsicum, and chillies)
Mongolian Sauce
Peking Sauce
(onion, celery, carrot, capsicum and shallots)
Ginger and Shallot Sauce
(ginger, shallots, onion, celery, carrot, zucchini baby corn and mushrooms)
Sweet and Sour Sauce
(onion, celery, carrot, zucchini, capsicum, baby corn and mushrooms)

Meat

G.S.T. Included

Chicken $13.90
Beef $13.90
Pork Fillet $13.90
(not available for sweet & sour sauce | see house special)
Lamb $17.00
Combination $16.00
Squid $16.00
King Prawns $20.00
Mixed Seafood (king prawns & squid) $20.00
Duck (half boneless duck) $20.50
Mini Prawns $14.50

Extras

	Packed Separately	On the Meal
Cashew Nuts OR Almonds	$2.00	$1.50
Crispy Chow Mein Noodles (per pack)	$2.00	$1.50
All Sauces packed separately	$0.50	N/A

House Specially

G.S.T. Included

Honey Sauce with king Prawns (deep fried) $20.00
Honey Sauce with Chicken (deep fried) $13.90
Lemon Sauce with King Prawns (deep fried) $20.00
Lemon Sauce with Chicken (deep fried) $13.90
Lemon Sauce with Duck (deep fried) $20.50
Steamed Duck with Crab Meat Sauce & Vegetables $20.50
Chilli Hot Duck with Vegetable (deep fried) $20.50
Sweet & Sour Pork deep fried with Vegetables $13.90

Omelettes

(egg, onion, celery, peas and bean sprouts)

Mini Prawn Omelette $14.50
Ham Omelette $14.50
Combination Omelette $14.50
King Prawn Omelette $18.00
Vegetable Omelette $14.50

Chow Mein

Broccoli, onion , Celery, Carrot, Baby Corn and Mushrooms served with Crispy Noodles
Price of Meat (Plus) $1.50

Asian Dishes

Singapore Noodles $15.00
Deep Fried Tofu with Spicy Sauce $14.00
Chinese Vegetables in Oyster Sauce OR Garlic Sauce
- Bok Choy $13.50
- Bok Choy and Broccoli $13.50

Thai Sauce with Deep Fried Chicken $13.90
Thai Sauce with Deep Fried Tofu $14.00
with Thai sauce or spicy salt
Green Curry OR Yellow Curry with Vegetables and
- Chicken $13.90
- Beef $13.90
- King Prawns $20.00

Informed Consent Models

- Opt-In
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- Disease/Study Specific
- Tiered Consent
- ***Broad Consent***
- Dynamic Consent

Broad Consent

- Specimens Collected for Planned Research, but……
- Scientific Goals/Technology Change with Time.
- Can consent be obtained at the time of enrollment that is ***Broader*** than a specific research protocol?

Broad Consent

- Under certain limited circumstances, the HHS and FDA Protection of Human Subjects Regulations at 45 CFR 46.116 and 21 CFR 50.25, respectively, permit an IRB-approved informed consent to be broader than for a specific research study. For example, when obtaining biological or tissue specimens from living individuals to create a repository established and maintained for research purposes, the IRB-approved informed consent document may include a description of the specific types of research to be conducted using the data and specimens maintained for the repository.

http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp

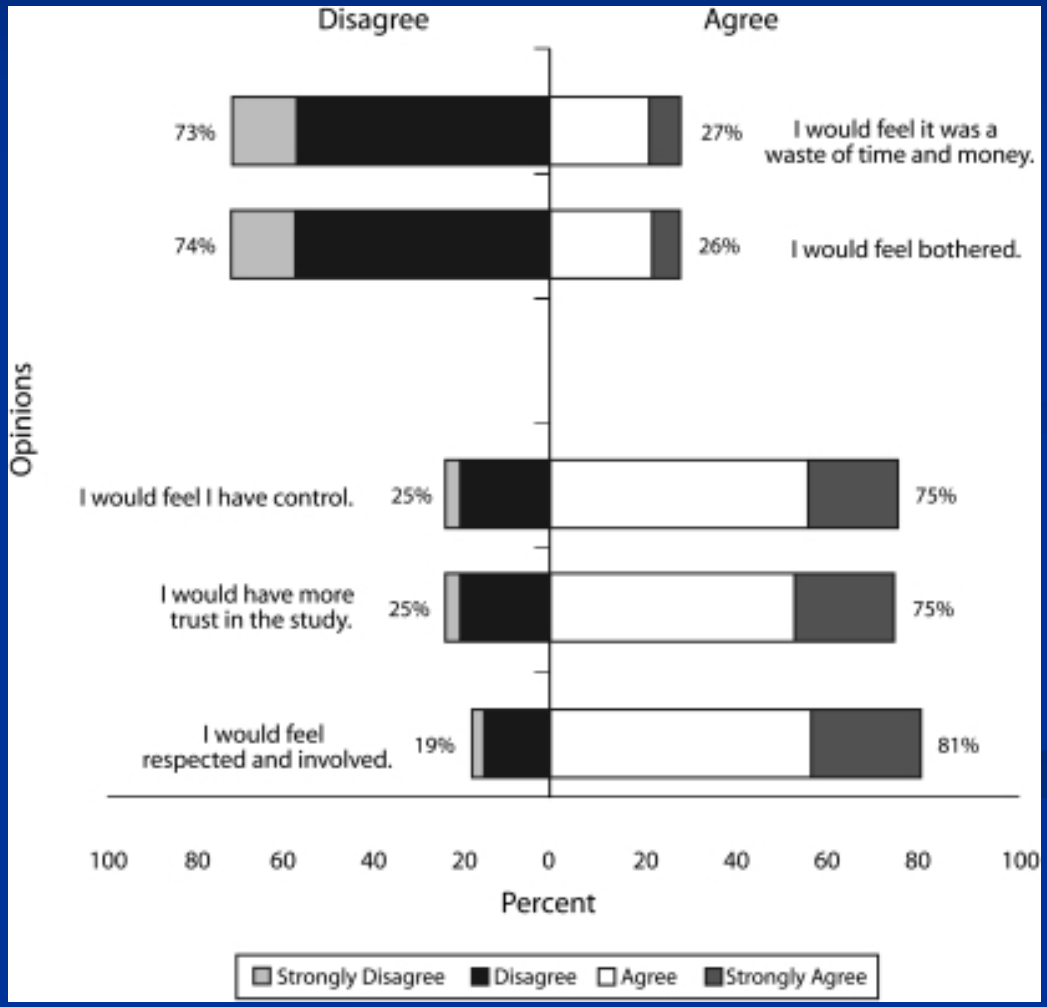
Informed Consent Models

- Opt-In
- Opt-Out
- Disease/Study Specific
- Tiered Consent
- Broad Consent
- ***Dynamic Consent***

How would you feel if you had to give permission to use samples and information before each research project?

- NIH Genomic Biobank
- 500,000 Individuals
- Baseline health exam
- Donate Specimens
- Access to Medical Records

- 16 Focus Groups
- 177 Item Online Survey
- Broad Consent?
- Menu Driven Consent?



Murphy J et al. Am J Pub Health 2009,99:2128-34.

How would you feel if you had to give permission to use samples and information before each research project?

- If I agree to the study I going to agree to just give my information and be done with it – however you want to use it. (Broad)
- I don't want to be contacted each time because there's going to be millions and millions of people wanting my DNA .(Broad)
- To call me every single time a researcher wants to do a study – I would rather have a list of things I don't want to be involved in. (Disease Specific/Tiered)
- It would be nice knowing every time someone is going to get your permission (Dynamic)
- I would rather sign a piece of paper than you take it upon yourself to do whatever. (Study Specific/Dynamic)

Murphy J et al. Am J Pub Health 2009,99:2128-34.

"Best" Informed Consent??

- For NIH funded research, investigators are expected to obtain consent for future uses and broad sharing of genomic and phenotypic data.
- Broad Consent maximizes the utility of collected samples and/or data.

http://www.genome.gov/27559024#_Broad_vs._specific

"Best" Informed Consent??

- Writing consent forms that offer multiple options can be challenging.
- Investigators should ensure that any choices participants can make are clearly described, consistent over time, non-conflicting, and understandable by future researchers.

http://www.genome.gov/27559024#_Broad_vs._specific

OHRP: Biospecimen Consent

- A clear description of the operation of biospecimen resource
- Conditions under which samples/data will be released to investigators
- Procedures for protecting privacy of research participants
- Description of nature/purpose of research
- Consequences of DNA typing, if planned

http://biospecimens.cancer.gov/bestpractices/elp/ic#c-2-2

Ethical Challenges/Controversies

- Informed Consent
- ***Confidentiality; Breach of Privacy***
  - Genetic Discrimination
    - Finance, Insurance, Employment
- Ownership and Commercialization

Risks of Biobanking

- Loss of Confidentiality
  - Stigmatization or privacy loss in the workplace
  - Financial discrimination
  - Insurability

PHI: Case Study

- Janet: 36 Y.O. HR specialist: 12 years experience applies for new position.

Is this Legal ?

- Pre-employment H&P reveals Janet's sister has breast CA, BRCA-1 positive.
- A similar applicant, w/o health concerns is hired instead.

Protection from Discrimination

- Genetic Information Nondiscrimination Act of 2008 (GINA)
- Prevents discrimination from health insurers and employers.
- *Does not Prevent* discrimination from life or long-term care insurers.
- Lessens concerns about Genetic Testing
- Encourages participation in research protocols

NCI: Privacy, Confidentiality

http://biospecimens.cancer.gov/bestpractices

- Establish clear polices to protect confidentiality of identifiable information.
- Certificates of Confidentiality available
- Document policies for maintaining privacy.
- Comply with state/federal regs re: privacy
- Biospecimen resources should use a system of data access with defined levels of access.

Should Research Data be Disclosed to Subjects??

- Preliminary/incomplete results could prove misleading/distressing.
- Genetic results have privacy implications for family members.
- Most labs are not CLIA certified.

Maschke KJ. Biobanks: DNA and Research. Hastings Center 2008;11-14

Should Research Data be Disclosed??

- NHLBI Working Group
  - **Researchers should disclose results of genetic studies when the associated risk for the disease is significant, the disease has important health or reproductive implications and when proven therapeutic or preventive interventions are available.**

Maschke KJ. Biobanks: DNA and Research. Hastings Center 2008;11-14

Should Research Data be Disclosed??

- NHLBI Working Group
  - **The exceptions to this recommendation are genetic – related diseases such as Huntington Disease that, although untreatable, have reproductive implications.**

Maschke KJ. Biobanks: DNA and Research. Hastings Center 2008;11-14

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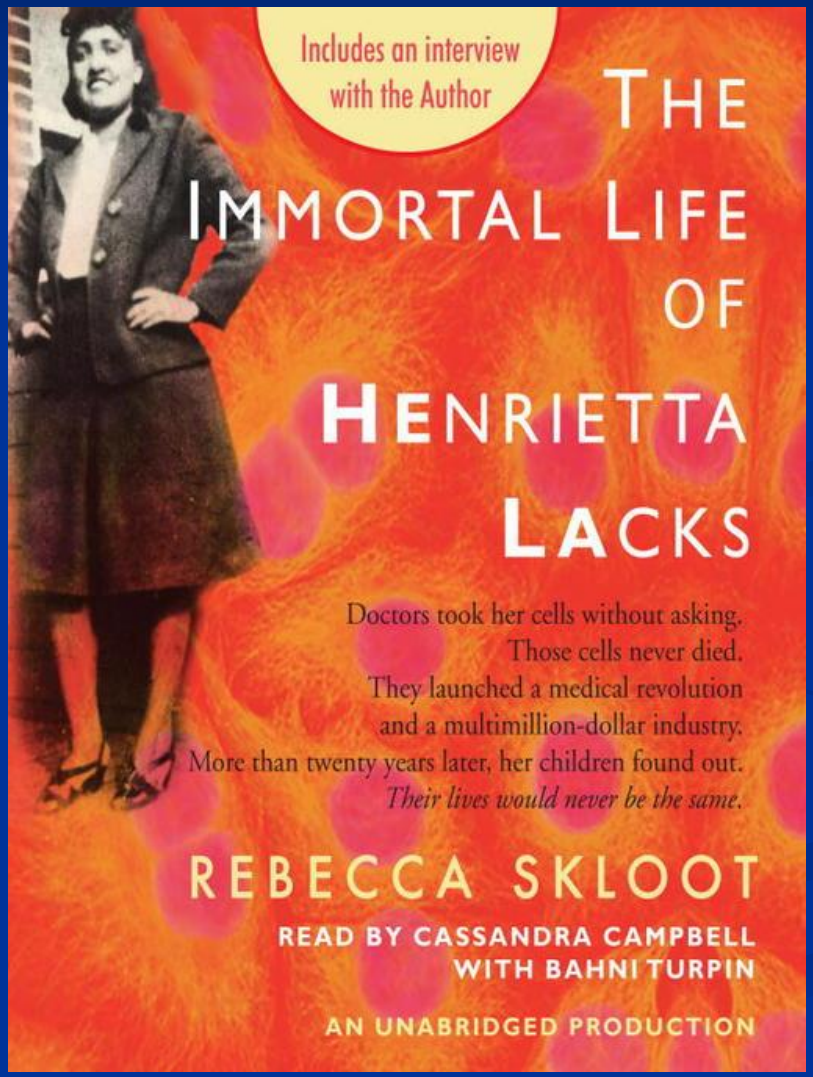
Ownership of Data/Samples



Ownership of Data/Samples

- Case Law
  - **Moore v Regents of University of California**
  - **Greenberg v Miami Children's Hospital Research Institute, Inc**
  - **Washington University v Catalona**

Conclusions

- Biobanks/Genetic testing here to stay
- Does every participant in a research trial need to participate in banking?
- "Informed" Consent Problematic
- Specific guidelines for broad consent for federally funded protocols.

Informed Consent: The Six W's

- *Why* am I being asked to participate?
- *What* samples will be collected?
- *Where* will the samples be stored?
- *Who* will have access/own my samples?
- *Will* I (*or others*) be notified of findings?
- *When* will I be asked to participate again?

Thank You!

UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

HRPO