Ellen Wright Clayton, MD, JD
Center for Biomedical Ethics and Society
Vanderbilt University

Ethical Challenges in Genome-Based Cancer Research
Liability and Other Challenges

Two Large-Scale Surveys on Community Attitudes Toward an Opt-Out Biobank(2011)

Nashville Community Health Survey N(%)		Vanderbilt Faculty and Staff Survey N (%)	
DNA biobank research is fine as long as people can choose not to have their DNA included.		*DNA databanks with all identifying information removed are fine as long as people can choose to opt out of having their DNA included.*	
Responses	*629*	*Responses*	*4033*
Somewhat or Strongly Agree	590 (93.9)	Strongly or Somewhat Agree	3816 (94.6)
Somewhat or Strongly Disagree	38 (6.1)	Somewhat or Strongly Disagree	217 (5.4)
You are comfortable with your DNA being used for research as long as personal information that can identify you is not included		*DNA databanks are fine as long as all identifying information is removed.*	
Responses	*639*	*Responses*	*4037*
Somewhat or Strongly Agree	557 (87.3)	Strongly or Somewhat Agree	3766 (93.3)
Somewhat or Strongly Disagree	81 (12.7)	Somewhat or Strongly Disagree	271 (6.7)
If all personal information is removed, researchers should be able to use leftover blood for research that has been approved by an ethics review board.		*DNA databanks with all identifying information removed are fine as long as an ethics review panel approved research with DNA in the databank*	
Responses	*630*	*Responses*	*4020*
Somewhat or Strongly Agree	557 (88.5)	Strongly or Somewhat Agree	3682 (91.6)
Somewhat or Strongly Disagree	73 (11.5)	Somewhat or Strongly Disagree	338 (8.4)

What do community members think?

How confident are you that research hospitals such as Vanderbilt Medical Center do a good job of protecting patients' medical information?		How confident are you that Vanderbilt Medical Center adequately protects patients' medical information?	
Responses:	639	Responses	4,026
Somewhat or Very Confident:	603 (94%)	Somewhat or Very Confident	3,713 (92%)
Only a Little or Not at All Confident:	36 (6%)	Not very or not at all confident	217 (5%)
		Don't Know	96 (2%)
How confident are you that your identity is protected when genetic information is used for research?			
Responses:	614		
Somewhat or Very Confident:	546 (89%)		
Only a Little or Not at All Confident:	69 (11%)		

What participants say about data sharing

- eMERGE
  - Marshfield -- 1/12,500 opted out of data sharing
  - Vanderbilt -- ~88% neutral or stated that data sharing increased willingness to participate
  - GHC – 86% consented to data sharing
  - General support in other eMERGE sites
  - Concerns about
    - Location within government
    - Identified need for public education
    - Use by for profit entities

Liability and ROR (1)

- Variants in genes that are the target of the research
  - Return is particularly appropriate where the purpose of testing is to guide experimental therapy
    - Ongoing debate about extent to which CLIA requirements apply
    - Questions have recently been raised about potential liability for returning inaccurate results from current public databases. http://www.genomeweb.com/print/1348716?utm_source=SilverpopMail

Liability and ROR (2)

- Variants that were not the target of the research
  - Non-targeted findings necessarily made in the course of research
    - "Stumbled upon"
    - Pleiotropic effects, e.g., pharmacogenomic
  - Incidental or secondary findings

Liability and ROR (3)

- Very few courts have held that physicians can be liable for failing to identify or act upon incidental findings *even in the clinical setting*
  - Lack of duty
  - Lack of breach of standard of care
    - Ellen Wright Clayton, Susanne Haga, Patricia Kuszler, Emily Bane, Krysta Shutske, Wylie Burke, Managing Incidental Genomic Findings: Legal Obligations of Clinicians, Genetics in Medicine 2013; 15: 624-629
  - The bar should be higher for research
    - Amy L. McGuire, Ellen Wright Clayton, The Legal Risks of Returning Results of Genomics Research, Genetics in Medicine 2012; 14(4):473-7

Liability and ROR (4)

- Increasing consensus that there is no duty in research to hunt for variants beyond the targeted genes
  - Presidential Commission for the Study of Bioethical Issues, Anticipate and Communicate
  - Paper led by Gail Jarvik for eMERGE and CSER ROR consortia

  - Both of these specifically reject expanding ACMG clinical recommendations to the research setting
  - Raises questions about earlier positions

Liability and ROR (5) – informed consent

- Clear consensus that research participants should be informed if return of results is contemplated
- If the possibility of ROR was not disclosed prior to research,
  - Impact on scope of disclosure?
  - Impact of unwanted disclosure?

- The impact of ROR on the research process is reason for caution

Some thoughts about broad consent for research and data sharing

- ANPRM would require consent for all uses of biospecimens on grounds that DNA is identifiable *per se*
  - Fails to address the fact that clinical information is often more identifiable
  - Represents a dramatic change from current practice that threatens much of epidemiology, particularly if unwarranted genetic exceptionalism is acknowledged
  - Clayton, Biospecimen Exceptionalism, The Future of Human Research Subjects Regulation, Cohen and Lynch, eds., MIT Press, in press, 2014

Some thoughts about broad consent for research and data sharing

- ANPRM favors broad consent for research
  - Contemplates "a standard, brief general consent form allowing for broad, future research"
  - Specifically does not apply when ROR will occur so potentially of little applicability
  - http://www.gpo.gov/fdsys/pkg/FR-2011-07-26/html/2011-18792.htm

Recent NIH data sharing proposal is premature

- Broad consent for research and data sharing is a factor to be considered by NIH in awards with few exceptions
  - Participants can decide about open v. controlled access
  - Federal Register 78(183): 57860-5 (Sept. 20, 2013)

- Systematic review reveals substantial variability in participants' stated desires for control over research use and their willingness to accept broad consent
- Plans are currently underway to survey 16,000 people at eMERGE sites about the acceptability of broad consent for research and data sharing

Conclusions

- Embracing ROR in research will increase the potential for liability
- Individuals should be protected from unwarranted re-identification of **all** research data
  - Genetic/biospecimen exceptionalism is not appropriate
  - The real question is what oversight and accountability are needed
- Broad use and data sharing are highly desirable, but questions remain about acceptability