SUMMARY STATEMENT

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(Privileged Communication)

Release Date: **02/25/2016 07:39 AM**

Revised Date:

Application Number: **1 R01 HG008988-01A1**

Principal Investigators (Listed Alphabetically):

BROTHERS, KYLE BERTRAM (Contact)
GOLDENBERG, AARON J

Applicant Organization: UNIVERSITY OF LOUISVILLE

Review Group: **ZRG1 SEIR-R (01)**
Center for Scientific Review Special Emphasis Panel
Societal and Ethical Issues in Research

Meeting Date: **02/17/2016**
Council: **MAY 2016**
Requested Start: **07/01/2016**

RFA/PA: **PA14-276**
PCC: **X5NL**
Dual PCC: **W0DR**
Dual IC(s): **CA**

Project Title: **Addressing Ethical Challenges in Networked Biorepositories**

SRG Action: **Impact Score** Priority Score **Percentile** Percentile
Next Steps: **Visit http://grants.nih.gov/grants/next_steps.htm**
Human Subjects:
Animal Subjects:
Gender:
Minority:
Children:
Evaluative Info

Clinical Research - not NIH-defined Phase III Trial

Project Year	Direct Costs Requested	Estimated Total Cost
1	257,157	Estimated Costs
2	273,067	
3	278,441	
4	293,215	
TOTAL	1,101,880	

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.
EARLY STAGE INVESTIGATOR
NEW INVESTIGATOR

1R01HG008988-01A1 Brothers, Kyle

EARLY STAGE INVESTIGATOR
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RESUME AND SUMMARY OF DISCUSSION: This project will address the ethical and governance challenges arising from the use of multiple networked biorepositories. The project is significant and timely as it will have a high impact on the policies and practices in biobanking and on data sharing between institutes for health related research information. The investigators are outstanding with appropriate and complementary expertise for the project. A minor concern for the reviewers is that this is a complex project for these new investigators and the timeline for the project is tight. However, the majority of reviewers agreed that this concern is mitigated by the strong research team for the project. The investigators were responsive to the previous review and have strengthened their application. The project is innovative as it is the first to evaluate networked biorepositories and will use both retrospective and prospective data. Other strengths of the project include the refining of the best practice recommendations by holding focus group sessions with stakeholders and the multiple qualitative methods with a focus on deductive analyses. There are some minor weaknesses in the application. Some of the reviewers are concerned whether networked biorepositories have unique issues in comparison to stand-alone biorepositories. After discussion, the reviewers agreed that the logistics of networked biorepositories will most likely lead to intensified ethical issues that are not found in stand-alone biorepositories. The reviewers all agreed that this project from outstanding investigators will have a high impact on the policy and practice of networked biorepositories.

DESCRIPTION (provided by applicant): Individual institutions across the country have worked to support research in a wide variety of areas, including precision medicine research, by developing large biorepositories comprised of biospecimens and health data collected from local patients and controls. However, these local cohorts rarely provide the diversity and size needed to identify and study subsets of patients who share biological mechanisms for their disease, and are thus more likely to respond to the same targeted therapies. To address this need, researchers have begun to promote the networking of multiple repositories within or across multiple institutions. This networked biorepository approach makes it possible for researchers to access larger, more diverse sets of data and biospecimens in a way that leverages the research relationships that local institutions have built with their own communities of donors. In order for this approach to be successful, networked biorepositories need to address important ethical, legal, and social challenges. Networked biorepositories are comprised of diverse sets of specimens and data from different institutions, each with their own governance structures and donor needs. For these reasons, they encounter complex issues related to consent and donor permission, privacy and data security, and data access. These novel challenges have not previously been examined in detail, and best practices for addressing these issues through governance and oversight processes are lacking. This study will address these important needs through a rigorous, mixed-methods study of the perspectives and experiences of stakeholders currently engaged in designing, operating, and governing networked biorepositories. It will also aim to develop approaches to consent and donor permission, privacy and data security, data access, governance, and oversight that are most appropriate and effective for a variety of networked biorepository configurations.

PUBLIC HEALTH RELEVANCE: Networked biorepositories make it possible for investigators in a wide variety of research domains to access large, diverse collections of biospecimens and health data across multiple institutions. At the same time, they also raise complex issues related to consent and donor permission, privacy and data security, and data access. Developing a detailed account of these challenges and identifying appropriate solutions, including effective governance and oversight processes, will enable new and developing networked biorepositories to support important health research while at the same time meeting the needs of donors and protecting the interests of contributing institutions.

CRITIQUE 1:

Significance: 2
Investigator(s): 3
Innovation: 3
Approach: 2
Environment: 2

Overall Impact: This proposal is judged to have a high potential for impact. The significance of the project is high given accelerating efforts to develop large, networked biorepositories to support precision medicine research, particularly as NIH funding opportunity announcements for such networks place limited emphasis on exploring the potential ELSI dimensions of these networks in the context of precision medicine research. The investigatory team and environment – though not without potential weaknesses – is well situated to carry out the study and this revised application addresses sources of concern that were identified in the original submission. The addition of a normative core enhances innovation compared to the original submission. The approach remains strong overall, and the proposed 4 year timeline for completion of the study is judged to be a strength as it allows for the possibility of unexpected delays in fieldwork.

1. Significance:

Strengths

- The NIH continues to focus on networked biorepositories as a key element of the nation's biomedical research infrastructure
- Calls for development of such networked infrastructure have had only a limited focus on ELSI issues thus a need for independent research on this important topic

Weaknesses

- The current application focuses on biorepository networks that are of modest scale compared to those envisioned for precision medicine research in the near future thus potentially reducing generalizability of results

2. Investigator(s):

Strengths

- The investigatory team is strong in multiple fields related to empirical and normative investigation of biorepositories
- The team includes support from biorepository stakeholders and leaders at the study sites to facilitate research access

Weaknesses

- Two relatively junior investigators lead this complex project – a concern that has been mitigated to some extent in this revised application through the inclusion of more and more-experienced senior investigators.

3. Innovation:

Strengths

- Focus on emerging frontier of networked biobanks and understanding ELSI issues they create

Weaknesses

- Translational activities are proposed but greater innovation could be achieved if more ambitious plans were outlined for how these translational activities could be integrated into future biobank network activities.

4. Approach:

Strengths

- Combination of retrospective, prospective, and translational aims is a strength of the approach
- Use of multiple qualitative methods with an appropriate focus on methods that emphasize deductive analyses
- The focus on perspectives of non-donor biorepository stakeholders is explicitly addressed and justified
- Additional time devoted to data collection mitigates concern that logistical or other unavoidable delays will harm project progress

Weaknesses

- Identification of networked biorepositories could draw on addition resources such as specialty societies, e.g. College of American Pathologists
- The use of focus groups in aim 3 seems uninspired and given that group participants will be drawn from extant research sites it is not clear that these groups will add much value

5. Environment:

Strengths

- Links to biorepository networks at various stages of development (established, forming, new) and with different ownership configurations is a strength
- Resources from different core institutions is a strength

Weaknesses

- PI's at different institutions is a potential weakness

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

Inclusion of Women, Minorities and Children:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- Inclusion/Exclusion of Children under 21: Excluding ages < 21 justified scientifically

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

- The applicants have been highly responsive to comments on their previous submission.

Budget and Period of Support:

Recommend as Requested

CRITIQUE 2:

Significance: 1
Investigator(s): 2
Innovation: 1
Approach: 2
Environment: 1

Overall Impact: There is a strong likelihood that the results of this project — the first systematic study of networked biorepositories — will positively impact policy and practice in the domain of biobanking and perhaps beyond. Although ethical and governance issues related to biobanks have received a great deal of attention, the networking of multiple biorepositories enormously increases their complexity. Moreover, the findings and “best practice” recommendations should have relevance in other situations where institutions share health-related research information. The PIs are well-qualified, and the other members of the research team provide complementary expertise. The level of institutional support for the PIs is impressive. The study design is excellent. All in all, this a well-designed project on an increasingly important subject.

1. Significance:

Strengths

- Given the need for larger and more diverse biorepositories (in order to identify subsets of patients who share the same biological mechanism for a disease), the networking of biobanks, both within and across institutions, is becoming increasingly common.
- Such networking adds a new level of complexity to the ethical and governance challenges associated with conventional biobanks. Although many of the ethical challenges relate to standard human subject protection concerns (around informed consent, privacy, return of research results, etc.) they are exacerbated in this context.
- As a prior reviewer noted, shared data sets that combine cohorts from different institutions are increasingly used in health research generally; thus project findings and recommendations are of potential significance beyond biorepositories.

Weaknesses

- The effort to explain why the ethical issues are different in kind (as opposed to degree) from those encountered in conventional biobanking seems forced and is unconvincing.

2. Investigator(s):

Strengths

- Both PI Kyle Brothers and MPI Aaron Goldenberg have strong records of research and publication and considerable prior experience with projects related to biorepositories.
- They have successfully collaborated previously.
- The other members of the research team (Richard Sharp, Jean Cadigan, Mark Rothstein, Heather Harrell, and Suzanne Case) provide complementary methodological and subject-related expertise. Addition of Eric Juengst to the Advisory Committee and Normative Core will provide greater depth in respect to ethics.

Weaknesses

- This is a very complex project, involving two geographically-separated institutions. Managing the project could be a challenge for new and early-stage investigators.

3. Innovation:

Strengths

- First systematic study to explore the challenges of networked biorepositories.
- Combines retrospective data obtained from interviews with prospective data obtained through participant observation.

Weaknesses

- None noted

4. Approach:

Strengths

- Makes use of different types of data (interviews, participant observation, focus groups).
- Will develop “best-practice” recommendations and refine them through focus group sessions with stakeholders.

Weaknesses

- None noted

5. Environment:

Strengths

- Both PIs are in institutions with excellent scientific environments and resources.
- Both PIs are strongly supported by their institutions.

Weaknesses

- None noted

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

- Risks are minimal.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Inclusion of Women, Minorities and Children:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- Inclusion/Exclusion of Children under 21: Excluding ages < 21 justified scientifically
- Will use purpose sampling in order to obtain a sample that is @ 25% minority and 50% female.

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

- The PIs have responded thoughtfully and adequately to all of the criticisms from the prior review and, in particular, to those related to a perceived lack of normative analysis.

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3:

Significance: 4
Investigator(s): 2
Innovation: 3
Approach: 4
Environment: 2

Overall Impact: This application describes an incredibly ambitious and complex multi-institutional research program designed to identify and address the unique ethical and regulatory challenges faced by networked biorepositories. While the research team is strong and has the expertise to carry out the work described, the timeline is likely unrealistic and the program of work overly ambitious. Further, additional work needs to be done to identify the unique ethical (rather than logistical or practical) challenges faced by networked biorepositories beyond those faced by stand-alone biorepositories, about which there is a rich literature.

1. Significance:

Strengths

- Research in precision medicine will increasingly depend on the combination of cohorts from multiple institutions – the PMI explicitly calls for this – making this proposal very timely and also giving it the potential to have immediate policy impact.

- The networked biobanks involved in the project are an already identified stakeholder group that could readily take up and implement the empirically-based, well-vetted recommendations of the sort planned.
- The “deep dive” described to identify and explore dissenting views would be new data with broad implications.

Weaknesses

- Better arguments or pilot data are needed to support the claim that unique issues are raised by the networking of biorepositories.

2. Investigator(s):

Strengths

- The team of investigators has the right combination of experience and expertise to successfully carry out this project.
- The team of investigators have solid records of funding and publications in areas relevant to the current proposal.
- The PIs have complementary expertise.
- The joint leadership plan seems reasonable.

Weaknesses

- The PIs have a developing collaborative relationship, but have not yet produced joint publications and have not managed research projects together in the past.

3. Innovation:

Strengths

- The methods used to address the three project aims will provide different and complementary kinds of data.
- The longitudinal ethnographic observation planned for Aim 2 is a relatively innovative method to assess the challenges, problem solving and resolution of challenges raised by networked biobanks.
- The “deep dive” described to identify and explore dissenting views is novel and may uncover important and previously undescribed perspectives.

Weaknesses

- None noted

4. Approach:

Strengths

- The methods described are appropriate and will provide complementary data

Weaknesses

- The proposal describes more work than can be done in the time allotted.
- Observation is a huge amount of work, and details are unclear (e.g., how many observations will there be at each site per week? What percentage of meetings/calls will be observed at each site?).

- Given the amount of work described, it appears that not enough effort is planned, raising the question of whether the work can be completed by the personnel on the proposal.
- The proposed timeline of work does not make sense and is not justified (e.g., transcription and analysis are not scheduled to begin until a year into data collection; recommendations are being developed 18 months before data collection is complete).

5. Environment:

Strengths

- The Investigators' home institutions are well equipped to support the research and administrative demands of this proposal.
- The CWRU Center for Genetic Research and Law, the Center for Individualized Medicine Bioethics Program at Mayo, and the Center for Genomics and Society at UNC-Chapel Hill will be able to provide ample supplementary expertise and support for the project.

Weaknesses

- None noted

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

- This is a low-risk protocol and protections described are adequate.

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Inclusion of Women, Minorities and Children:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- Inclusion/Exclusion of Children under 21: Excluding ages < 21 justified scientifically
- Recruitment plan is adequate and scientifically justified.

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Budget and Period of Support:

Recommended budget modifications or possible overlap identified:

- Insufficient effort is planned for the PIs, given the amount of work proposed.

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE

INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE

INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE

INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1 R01 HG008988-01A1; PI Name: Brothers, Kyle Bertram

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.