The Role of P3G in Encouraging Public Trust in Biobanks

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Abstract A key element in the success of a biobank is the trust and support of the public. Building this trust is a difficult process. The field of population genomics raises many ethical and societal issues that must be addressed in order for the public to see participation as a trustworthy activity. The Public Population Project in Genomics (P3G) is an international collaboration dedicated to bringing members of the population biobanking community together to share their expertise for the advancement of population genomics research. Through its fundamental principles of promotion of the common good, responsibility, mutual respect, accountability and proportionality, P3G seeks to create tools and resources to assist those involved in biobanks to conduct their research in such a way as to inspire the trust and participation of the public.

1 Introduction

One key element in the potential success of any biobank is the trust and support of the public (Williams and Schroeder 2004). Potential participants need to trust that the research is useful and that they will not be harmed through their participation. The community or population in which the biobank is involved must approve of its plans and its impact. If the biobank is publically funded, community leaders and funders must agree that this effort is worthy of their resources. Finally, society in general must accept that these scientific efforts are beneficial and in the best interest of the public.

Building and maintaining trust is a difficult process. Population-based genomics, like other fields of scientific research, has special issues that must be addressed. These include the use of human tissue, confidentiality, and the return of results from DNA studies. As Beskow has noted, in light of a history of research abuses and a continued belief in genetic determinism, "… clarifying the duties of investigators to participants in population-based research in genomics is important." (Beskow 2004) It is therefore vital to assist investigators and researchers to conduct their research to a high standard that will justify the trust of the public.

The Public Population Project in Genomics (P3G) is an international collaboration dedicated to bringing members of the population biobanking community together to share their expertise for the advancement of population genomics re-

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search. By creating a repository of resources and tools, by collaborating on research projects and by promoting the sharing of knowledge, it is creating an infrastructure to encourage interoperability in human population genomics as well as a resource for information on best practices in this field. This paper will discuss how P3G, by providing these tools and resources, seeks to help those involved in biobanks to conduct research of high quality that will inspire the trust and participation of the public.

2 Background of P3G

P3G was formally launched, after three years of planning, in May 2007. (P3G 2007a) P3G is not itself a biobank and does not collect data and samples from participants. It works with those involved in biobanking,

… to create, harmonize and share methods, tools and information so as to enhance the design of emerging biobanks and to promote compatibility – between studies – of data (e.g. socio-economic and clinical), samples, and supporting infrastructure (e.g. sample and data-management systems) (Knoppers et al 2008).

In recent years, since the sequencing of the human genome, there has been a move towards "… studying the genetic architecture of complex diseases …" (Smith et al. 2005). With advances in genetic technologies and the increasing availability of genetic information from individuals, studying gene-gene, gene-disease and gene-environment interactions is now possible. Large cohort studies (prospective studies following a large group of people over years) have been in existence for many years. As well, new large-scale population resources, such as CARTaGENE and UK Biobank, are being created (CARTaGENE 2008, UK Biobank 2007). Access to large and well-characterized sets of data provided by such resources has enabled researchers to identify genetic variants related to health and disease (GAIN Collaborative Research Group 2007, Wellcome Trust Case Consortium 2007). While individual biobanks will undoubtedly produce discoveries regarding health and disease, it is now recognized that by pooling data between population resources, it is possible to investigate not only rare diseases but also common complex diseases, with greater confidence and in greater detail. It is P3G's goal to assist biobanks to share these resources.

P3G comprises members from 25 countries, in three membership categories: Charter, Associate and Individual (P3G 2008e). The founding member biobanks were CARTaGENE (Quebec, Canada), the Estonian Genome Project and GenomEUtwin (involving 8 countries conducting twin studies). Other member biobanks represent Europe, North and South America, Africa, Asia and the Pacific.

International Working Groups (IWGs) of P3G carry out its scientific development work. There are currently 4 IWGs: Social, Environmental and Biochemical Investigations (IWG1); Information Curation and Information Technology (IWG2); Ethics, Governance and Public Engagement (IWG3); and Epidemiology

and Biostatistics (IWG4). Research 'Cores', which are independently and externally funded research projects, work with the IWGs and address issues related to biobanking, such as policymaking, health systems research and methods for harmonizing and integrating data. Data and tools created by the Cores are housed in the P3G Observatory (P3G Observatory 2008a), a repository of resources for the use of the community. All resources are publically available.

Underpinning these activities is the P3G Charter of Fundamental Principles aimed at promoting ethical comportment and scientific integrity:

- Promotion of the common good – P3G will optimise the benefits of collaborative research for the benefit of all.
- Responsibility – Protection of the interests of all affected stakeholders including families, groups, populations, researchers and research sponsors is the highest priority. Every effort will be made to respond to the concerns of stakeholders in a timely and appropriate manner.
- Mutual respect – The development and sustainability of P3G is based on responsibility, collaboration, co-operation, trust and mutual respect for others, which includes recognition of cultural diversity and the scientific specificity of the projects involved.
- Accountability – All standards, processes and procedures will be transparent and clear, developed on the basis of consensus, and aim to create best practice in the networking of population genomics resources.
- Proportionality – All research materials (such as data and samples) must be protected to the highest standards of privacy and propriety, while at the same time allowing and promoting the free exchange of ideas, data sharing and openness for the benefit of all. (P3G 2008a)

In adhering to these principles, P3G can work internationally, "… span[ning] critical boundaries across cultures and between legal systems."(Knoppers et al. 2008)

3 Trust Building

When individuals agree to participate in research, they trust that their contribution, such as tissue or information, will be used in an ethical manner. A set of criteria for 'ethical' clinical research suggested by Emanuel and colleagues includes value, scientific validity, informed consent and respect for potential and enrolled subjects (Emanuel et al. 2000). These criteria can also be applied to population research. It is the role of P3G to assist researchers to achieve the highest scientific and ethical standards through the creation of tools for use by the biobank community, to build consensus on best practices in the field, and to transfer that knowledge to the general research community. Specific examples will demonstrate the application of P3G's fundamental principles in these areas. Further, recognition of the necessity and practicability of a platform of scientific communication is re-

flected in the development of a common lexicon to promote the understanding of key definitions and issues involved in population genomics (P3G 2007b).

3.1 Promotion of the Common Good

P3G is founded on the principle that scientific knowledge is a common good belonging to humanity (Knoppers and Joly 2007). Inspired by the 2002 Statement on Genomic Databases of the Human Genome Organisation (HUGO), which maintains that databases of primary sequences are 'global public goods' (HUGO 2002), the objective of P3G is to ensure that access to genomic information is open to all, and for the benefit of humanity. One of its priorities, therefore, is the creation of tools to foster international interoperability. It encourages, for example, the formulation of broad consent regarding participation in the construction of population biobanking resources; it also affirms the right of members to access, including international access, thereby ensuring that raw data produced by such resources remains in the public domain.

3.2 Optimizing Collaborative Research

P3G, through its IWGs and Cores, works on the many different methodological issues that arise in the creation and running of population biobanks. A large number of samples may be required, for example, as in the population studies noted earlier, to confirm causal links between genes and disease (Smith et al 2005). It can be difficult to share data across studies because while the research question may be the same (whether identical twins who smoke develop a particular cancer at the same rate); the information sought and collected (the quantity of cigarettes smoked) may be collated and recorded in different ways (by the number of cigarettes, the number of packs of cigarettes, etc.). When data is formatted differently, it is not easily shared across platforms. In order to address this problem, P3G is collaborating with other organizations on the DataSHaPER (Data Schema and Harmonization Platform for Epidemiological Research) project. This project is creating a tool that includes

> a comprehensive set of variables that ought ideally to be collected by large epidemiological studies and biobanks whenever the fundamental aim is to undertake general-purpose biomedical research (P3G 2008b).

Such a tool will enable biobanks to harmonize some or all of the data they will collect by allowing them to collect information by reference to the same set of variables, increasing the potential for sharing of information and thus the statistical power of their studies. Hopefully, the tool will also help those designing new

biobank infrastructures to 'build in' the ability to share data from the beginning of their study. This should optimize the efficiency of the infrastructure by broadening the scope of research conducted and reducing the number of samples required.

Another project, led by a Core at the UK DNA Banking Network, is the DNA Quantity and Quality Control (Q2C) project (UDBN 2008). Q2C seeks to harmonize DNA measurements among laboratories internationally, thus facilitating the movement of samples between laboratories. As research groups around the world are increasingly sharing DNA, it very important to ensure that measurements are consistent. Such projects should improve the ability of biobanks to collaborate with others.

More generally, the P3G Observatory houses data and tools created by the Cores, as well as information related to population research. The Observatory Study Catalogues contain general information, for example, on 122 new, on-going or completed biobank studies from around the world (P3G Observatory 2008c).[1] It also has a repository of pro forma biobank questionnaires (P3G Observatory 2008b) for use as a reference tool, enabling researchers to compare and contrast the research being conducted by various biobanks.

3.3 Responsibility

It is important to P3G to protect the interests of all stakeholders in biobanks. The IWG3 has accordingly created generic consent materials for population biobanks (Wallace et al 2008), by synthesis of the materials of a group of P3G members. The materials include an information pamphlet and consent form that are to act as templates for identification of issues to be considered by biobanks when preparing their own materials. 'Fill-in' boxes allow the templates to be customized by the designer, according to the structure and needs of the new biobank. The templates are publicly available at the P3G Observatory (P3G 2008c), but their use by P3G members is not mandatory; they are merely tools for the assistance of the biobank community and other interested parties.

Future work of the IWG3 will focus on governance and access issues from the perspectives of stakeholders. The arrangements for governance of a biobank can directly affect participation; systems of ethics oversight and research regulations have been shown to contribute to the level of security that participants feel about the research (Dixon-Woods et al 2007). Access to samples and data is important, both to participants, who wish to be fully informed about the uses to which their contribution is being put, and to researchers, who cannot share without participant consent and mechanisms, such as material transfer agreements, being in place.

[1] This number is accurate as of March 2008.

3.4 Mutual Respect

Many organizations around the world are involved in setting standards and creating policies in the field of population biobanking. Working in the area of science and ethics of population genetic databases, to name just a few, are the World Health Organization, the International Society for Biological and Environmental Repositories (ISBER) and the United Nations Educational, Scientific and Cultural Organization (UNESCO) (P3G 2008d). Other projects developing standards for biobank researchers include: Promoting Harmonisation of Epidemiological Biobanks in Europe (PHOEBE), the European Network of Genomic and Genetic Epidemiology (ENGAGE) and the pan-European Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) (BBMRI 2008, ENGAGE 2008, PHOEBE 2008). In light of the number of organizations issuing policies, guidelines and standards, there is naturally a concern that there will be confusion among the scientific, ethics and policy communities as to which policies or standards ought to be followed. As a result, P3G and other groups have considered facilitating discussion among these various bodies in regard to their work, in order to identify opportunities to collaborate, as well as any gaps that may need to be filled or areas of overlap between them. This could help to ensure that existing projects are not duplicated and that potentially beneficial new initiatives are not lost, due to a belief that 'it's already being done.' It is also shows respect for public funds and contributions of samples and data, both of which are limited resources.

A particular question discussed within P3G has been whether adherence to standards developed by the organization will constitute a mandatory requirement for members. Operating on the fundamental principle of mutual respect, which recognizes the cultural diversity and scientific specificity of its member projects, the clear answer is that it has never been the intention of P3G to impose its standards or tools upon its member organizations. All tools are made publicly available, but their implementation by members is not obligatory. However, members have to adhere to the P3G Charter of Fundamental Principles when involved in P3G-related activities.

3.5 Proportionality

While governance is essential for maintaining public trust and participation, controls for the review of research protocols, for data and sample security, and for ongoing monitoring should be proportionate to the sensitivity of the data.

… "Whereas to determine whether a person is identifiable account should be taken of all the means likely reasonably to be used either by the controller or by any other person to identify the said person." This means that a mere hypothetical possibility to single out the individual is not enough to consider the person as

"identifiable". If, taking into account "all the means likely reasonably to be used by the controller or any other person", that possibility does not exist or is negligible, the person should not be considered as "identifiable", and the information would not be considered as "personal data" (EC 2007).

Thus, the more open aggregated databases anonymize data. Longitudinal studies, with coded samples that have more phenotypic data attached, require a higher level of security. P3G is constructing a typology of models of data security, access and governance that reflect this proportional approach.

4 Conclusion

The goal of P3G is to help researchers to harmonize aspects of their population genomics research in order to optimise it for the benefit of the public. It is not aimed at diluting that which is special, both culturally and scientifically, about a particular biobank project. Biobanks should differ, according to the needs and questions that will benefit a particular community. But what can be learned from individual communities can also be of use to many others. Where sharing can occur and where harmonisation is possible, P3G will lead efforts to facilitate them. In this way, population biobank research can be used as effectively as possible to best serve the needs of the public. The public trusts that we will do no less.

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