EJHG Open

European Journal of Human Genetics (2013) 21, 243–244

www.nature.com/ejhg

NEWS AND COMMENTARY

P3G: return of results

Crossing the boundary between research and health care: P3G policy statement on return of results from population studies

Martina C Cornel

European Journal of Human Genetics (2013) **21,** 243–244; doi:10.1038/ejhg.2012.160; published online 25 July 2012

BIOBANKING: RESEARCH OR HEALTH CARE?

Biobanks collect biological samples and associated data for medical-scientific and diagnostic purposes and organize these in a systematic way for use by others.[1] Although the first goal of many biobanks is research, increasingly the boundaries between biobanking research and health care are becoming blurred. Some biobanks are collections of bodily materials from health-care settings (tumor samples, dried blood spot cards from neonatal screening). Here, research is a secondary goal: the material was first of all collected for health-care purposes. Some research biobanks give access to the results of (some of the) investigations in the interest of the participants, such as the Estonian biobank[2] and Lifelines in the Netherlands (http://lifelines.nl/), both members of the Public Population Project in Genomics (P3G) consortium (www.p3g.org).

P3G is an international not-for-profit consortium that encourages collaboration between researchers and biobankers and promotes harmonization. The activities include ethical, legal and societal issues on biobanks and population studies. Such a collaboration during many years made it possible to develop guidance with collective input of many biobanks in several challenging fields, such as informed consent and the return of results.

In this issue, the P3G consortium proposes an important step to cross the boundary between research and individual health care by proposing to consider to return incidental findings (IFs) to participants under certain conditions.[3] The statement regards population studies, where participants have agreed that their bodily material and information may be used for the advancement of science. They did not enter the health-care system with a question or complaint, but are (often healthy) volunteers that were altruistic.

ALTRUISTIC OFFER OR RETURN?

In the past, the default position for research projects was not to return any individual results to participants. Innovative research findings need other studies to confirm their validity. The research laboratories usually do not have the quality assessment required in health care. Also, the funding provided for research studies is often limited, so that recall of participants for individual genetic counseling may not be possible within the research budget.

In the age of genomics, proteomics, metabolomics and whole-genome sequencing, however, it is more than conceivable that a cancer predisposition is recognized when performing whole-genome analyses in a research setting.[4] Or, a mutation in the Duchenne gene is identified when looking for the cause of autism.[5] The identification of mutations (or other research findings) with clinical significance may lead to a conflict of interest in the researcher and/or the physician: how to balance the privacy and confidentiality on one hand to the right-to-know on the other hand.

In the P3G statement, several modalities to return results are discussed.[3] Findings at baseline should be returned as soon as possible, where relevant, encouraging the participants to contact a physician. Newsletters and websites may report general results. However, the innovative part of the statement regards the return of individual research results and IFs to participants.

IF CONSENTED, RETURN VALID AND ACTIONABLE RESULTS

An important question in the statement remains whether participants at recruitment consented (not) to return individual results.[3] Moving forward, adding a return policy option could be considered in any informed consent procedure. Return of results should be considered for actionable results that are analytically valid, according to the statement. In the example of cancer predisposition, where frequent colonoscopy could be offered for secundary prevention, return of results meets this criterion. This statement may be the start of a real paradigm shift: from biobanking to public health, moving away from strict boundaries between research, individual health care and screening to an integration of these functions.

For many common complex disorders, genetic tests are only clinically useful in 5–10% of cases, yet these are the cases that have most severe symptoms at a young age and profit most from prevention.[6] Starting to consider what P3G is proposing now will not revolutionize medicine immediately, yet it may contribute to translate genomics to public health.

RESEARCHERS' OPINIONS

Recently in this journal, Miller *et al*[7] reported on a survey among researchers working on autism spectrum disorders and cystic fibrosis. A total of 343 researchers from around the world answered the survey based on true-to-life vignettes. Many participants strongly endorsed information and care-based obligations for clinically significant findings. This will cascade into obligations after an initial report of results: researchers should ensure that participants gain access to updated information. They also perceived a range of barriers, restricting access to relevant clinical services, such as waiting lists, lack of clinical expertise and the cost of relevant

Martina C Cornel is at the Clinical Genetics/EMGO Institute for Health and Care Research, VU University Medical Centre, Amsterdam, The Netherlands.
E-mail: mc.cornel@vumc.nl

clinical services. Implementing the P3G statement into practice will thus require cascading out several other elements of a chain, from keeping in touch with families after a first report of a clinically significant research finding till (further) developing adequate health-care services.

FAMILY MEMBERS AND CHILDREN

The P3G statement limits its advice to individual participants.[3] If a Duchenne mutation would be found in a healthy woman, the risk would rather be a reproductive risk. Would the P3G statement consider this an IF where return of results should be considered? This is not immediately evident. Reproductive risks are a case for further policy development.

A related topic is the position of minors in population studies and biobanks. If research questions cannot be answered by a study of adults, minors need to be included. Here parents give informed consent for participation on behalf of their child. In a recent publication in this journal, Hens *et al.*[8] recommended, on behalf of the Public and Professional Policy Committee of the European Society of Human Genetics, that 'Biobanks should have a policy about returning information about preventable or treatable conditions of early onset when participants are minors. Details of this should be included in the consent forms', and 'The right of parents to receive or not to receive genetic information about their children is limited. In the rare case that information about a preventable or treatable early-onset disease is found, they should be notified regardless of their wishes providing the findings are subject to assessment of clinical validity and utility.' Especially for vulnerable persons, the balance between the right-to-know and the right-not-to-know needs separate assessment.

CONSORTIA

Investigators in biomedical research projects are first of all obliged to achieve their milestones in terms of finding genes, identifying the pathways, developing medication and publication of these results. All research, however, needs an infrastructure, local but preferably also international. A strength of P3G is that ethical, legal and social 'products' have also been developed in the consortium, for the benefit of the entire research community. P3G has to be congratulated on taking this role very seriously. Only through several years of discussion and reflection in a biobanking community, has the recent policy statement been developed.

There are further initiatives in this direction in the European context. ERIC is the European Research Infrastructure Consortium that will provide a legal structure for infrastructures that were lacking a legal entity. European countries will sign a memorandum of understanding to provide legal structures for the Biobanking and Biomolecular Resources Infrastructure and the European Advanced Translational Infrastructure in Medicine. Hopefully, these and similar consortia will pave the way for effective future research and its translation into optimal health care, respecting relevant ethical, legal and societal issues ■

CONFLICT OF INTEREST

MC is principal investigator in the Netherlands Center for Society and the Life Sciences (Nijmegen), supervising amongst others a project on biobanks: "Wealth of data - blurring boundaries between research and care", and chair of the Working Party of the Center for Medical Systems Biology (Leiden), both of which are funded by the Netherlands Genomics Initiative. She is also chair of the Netherlands Program Committee Neonatal Heelprick Screening.

1 European Commission. Biobanks for Europe. A challenge for governance. European commission, Directorate-General for Research and Innovation, Brussels. *ISBN* 2012; **978**, 92-79-22858-2.
2 Estonian Genome Project. Available at. http://www.biopark.ee/documents/Estonian_genome_project.pdf accessed 21 June 2012.
3 Knoppers BM, Deschênes M, Zawati MH, Tassé AM: Population studies: return of research results and incidental findings. Policy statement. *Eur J Hum Genet* 2012; doi:10.1038/ejhg.2012.152.
4 Schwarzbraun T, Obenauf AC, Langmann A *et al*: Predictive diagnosis of the cancer prone Li-Fraumeni syndrome by accident: new challenges through whole genome array testing. *J Med Genet* 2009; **46**: 341–344.
5 Pagnamenta AT, Holt R, Yusuf M *et al*: A family with autism and rare copy number variants disrupting the Duchenne/Becker muscular dystrophy gene DMD and TRPM3. *J Neurodev Disord* 2011; **3**: 124–131.
6 Becker F, van El CG, Ibarreta D *et al*: Genetic testing and common disorders in a public health framework: how to assess relevance and possibilities. Background Document to the ESHG recommendations on genetic testing and common disorders. *Eur J Hum Genet* 2011; **19** (Suppl 1): S6–S44.
7 Miller FA, Hayeems RZ, Bytautas JP: One thing leads to another: the cascade of obligations when researchers report genetic research results to study participants. *Eur J Hum Genet;* e-pub ahead of print 15 February 2012; doi:10.1038/ejhg.2012.24.
8 Hens K, Van El CE, Borry P *et al*: On behalf of the PPPC of the European Society of Human Genetics. Developing a policy for paediatric biobanks: principles for good practice. *Eur J Hum Genet* 2012; e-pub ahead of print 20 June 2012; doi:10.1038/ejhg.2012.99.