Pharmacogenomic Data Sample, Collection and Storage : Public Perception,Ethical Issues and Policy Approaches to the Problem

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Rome, October 2005

Outline

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I. Introduction

- Genomic profiling has the potential to usher in a revolution of personalized healthcare and disease prevention. But evidence to support genomic profiling is inconsistent, and data on the health outcome benefits based on such testing are lacking.

  For genomic profiling to become valid and useful, well designed epidemiologic studies and thorough clinical evaluations of recommended interventions based on genotype are required.

(Haga SB, Khoury MJ, Burke W, 2003)

I. Introduction

- [R]esearchers have become concerned with reducing the possibility of spurious associations due to population stratification , and increasing the efficiency of uncovering candidate polymorphisms and their interactions in different genes.

  Many have called for the creation of large databases that include genotypic data such as the deCODE genetics project and the emerging UK Biobank.

  Such data-bases would increase efficiency in conducting studies on disease association and drug response by providing much needed samples to be used in a broad range of research.

  (Soo-Jin Lee S, 2005)

II. Public Perception

Lack of large scale empirical surveys is problematic. Results are often contradictory making it difficult to find a common trend.

- Genetic information is generaly seen in the same light as health information though many believe it to be more fundamentally personal with more worrying implications for abuse **(Pollara-Earnscliffe, Canada, 2003)**

- Public has a somewhat greater confidence in pharmacogenomics research than in other types of genetic research **(Rothstein, Hornung, 2003)**

- General public knows little about the use of human biological samples **(Porter et al., 2000)**

II. Public Perception

- Public attitudes will play a crucial role in realising the potential of scientific and technological advances.

  Most participants engaged in the public dialogue commissioned as part of this study saw the potential development of pharmacogenetic testing as beneficial for helping people make informed choices.

  However, there were major concerns, including issues of consent and confidentiality in the handling of biological samples, and whether the Government and the healthcare system could successfully deliver genetic technology in the future.

  We recommend that the public should be regularly consulted about the applications of pharmacogenetics.

The Royal Society,

Personalised Medicines : Hopes and Realities, UK, 2005

II. Public Perception

3 genetic fallacies

- **Exceptionalism**
- **Determinism**
- **Generalisation**

III. Consent

- Consortium on Pharmacogenetics, *Ethical and Regulatory Issues in Research and Clinical Practice*, 2002.
- Pharmacogenetics Working Group, *Elements of Informed Consent for Pharmacogenetic Research*, 2002.
- World Health Organization (WHO), *Genetic Databases : Assessing the Benefits and the Impact on Human and Patient Rights*, 2003.
- UNESCO, *International Declaration on Human Genetic Data*, 2004.

III. Consent

- In most cases, a reasonable policy is to obtain consent to a range of related studies over a defined period of time, with special provision for specific consent for studies that may be especially problematic to the subject.

Consortium on Pharmacogentics, 2002

III. Consent

- Some existing guidelines state that the study subject has the right to decide (prospectively) the future uses of his sample.

  Such guidelines imply a requirement for recontact or re-consent.

  This option is not always practical or even possible and is dependent on the category and the relative anonymity of the genetic samples collected for a pharmacogenetic study.

Pharmacogenetics Working Group, 2002

III. Consent

- In some cases it might be desirable to seek broad, open-ended consent to future research, the purposes, limits or consequences of which are currently unknown.

  In such cases, blanket future consent is only permissible where anonymity can be guaranteed, and there is no risk that unexpected results will filter back to the subjects concerned.

  If this guarantee is not possible, or if linking of data is necessary for the research, then specific consent to the specific research must be obtained.

Word Health Organization, 2003

III. Consent

- Human genetic data, human proteomic data and the biological samples collected for [scientific research] should not be used for a different purpose that is incompatible with the original consent, unless the prior, free, informed and express consent of the person concerned is obtained or unless the proposed use, decided by domestic law, corresponds to an important public interest reason and is consistent with the international law of human rights.

UNESCO, 2004

IV. Data Protection

- Council for International Organizations of Medical Sciences, *International Guidelines for Biomedical Research Involving Human Subjects*, Geneva, 2002.
- World Health Organization (WHO), *Genetic Databases : Assessing the Benefits and the Impact on Human and Patient Rights*, 2003.
- European Society of Human Genetics, *Polymorphic Sequence Variants in Medicine: Techinical, Social, Legal and Ethical Issues Pharmacogenetics as an Example*, 2004.
- UNESCO, *International Declaration on Human Genetic Data*, 2004.
- Council for International Organization of Medical Sciences (CIOMS), *Pharmacogenetics: Towards Improving Treatment with Medicines*, 2005.
- PRIVIREAL, *Recommendations from PRIVIREAL to the European Commission*, 2005.

IV. Data Protection

It is recommended that

- Pharmacogenomic information should be considered part of the spectrum of all health information.
- Public policy should reject the notion of genetic exceptionalism derived from pharmacogenetics which, even if inadvertently expressed, will impede biomedical research and healthcare delivery.
- All genetic data, regardless of their apparent information content, should be treated with the same high standards of confidentiality as any other personal or medical data.
- Public policy should provide safeguards against the inappropriate use of medical data, including pharmacogenetic data.

CIOMS, 2005

IV. Data Protection

- "[…] even if there is no intention to do so, the use of the label "anonymisation" operates as a metaphor or an ideological tool to relieve researchers, at least in their own minds, from the need to comply with the law's demands."

PRIVIREAL, 2005

« Recommendations from PRIVEAL to the European Commission ».

IV. Data Protection

- If genomic screens such as microarrays become automated for large-scale use, it could entail data storage in enormous institutional information systems.

  It is also quite possible that the complexity of such results would mean that no one report or counseling session could truly convey all the results.

  Therefore, one may have to repeatedly refer to the database to harvest information – but if this becomes the case, where should the database be housed, and who should have access?

ESHG, 2004

IV. Data Protection

Article 16:

(a) Human genetic data, human proteomic data and the biological samples collected for one of the purposes set out in Article 5 should not be used for a different purpose that is incompatible with the original consent, unless the prior, free, informed and express consent of the person concerned is obtained according to the provisions of Article 8 (a) or unless the purposed use, decided by domestic law, corresponds to an important public interest reason and is consistent with the international law of human rights

UNESCO, *International Declaration on Human Genetic Data* (2003)

IV. Data Protection

- [T]he terminology used to ensure confidentiality mechanisms for samples and data in genetic research has become so 'babelesque' as to ultimately impede the sharing of research data.

  The cumulative effect of the efforts of various international organizations, including the World Medical Association, the Consortium on Pharmacogenetics, the Council for International Organizations of Medical Sciences (CIOMS), the Council of Europe and the European Society of Human Genetics have resulted in confusing, redundant and contradictory terminology.

(Knoppers BM, Saginur M, 2005)

IV. Data Protection

Simplified nomenclature for sample identifiability	
Coded (single/double)	Anonymized
•Identifiable	•Absolute anonymity
•Linked	•Unlinked anonymized
•Linked anonymized	•Non-identifiable
•Potentially identifiable	•De-identified
•Re-identifiable	•Irretrievably unlinked
•Pseudonymized	•Irreversibly de-identified
•Reversibly de-identified/anonymized	•Irreversibly unlinked
•Proportional anonymity	•Nonidentified
•Reasonable anonymity	•Permanent anonymization
•Traceable	•Unidentifiable
•Unidentified/unidentifiable for research purposes	•Unlinked

Knoppers BM, Saginur M. The Babel of genetic data terminology. Nat Biotechnol 2005;23(8):925-7.

V. Harmonisation

- HUGO, Statement on Human Genomic Databases 2002.
- ECOSOC, *Report of the Secretary-General on Information and Comments Received from Governments and Relevant International Organizations and Functional Commissions Pursuant to Council Resolution 2001/39*, 2003.

V. Harmonisation

- Despite the existence of numerous declarations, guiding principles and codes dealing with the issue of genetic data, changing conditions of genetic research call for the establishment of an international instrument that would enable states to agree on ethical principles, which they would then have to transpose in their national legislation.

ECOSOC (2003)

V. Harmonisation

- These changes concern the increasing involvment of the private sector, the rapidly growing number of genetic databases, the controversial nature of certain of the intended applications[…], the increasingly international nature of genetic research and the cross-border flow of genetic data.

ECOSOC (2003)

V. Harmonisation

- The free flow of data […]should be encouraged. (art.3)
- [t]he free flow, access, and exchange of data are essential. Cooperation and coordination between industrialized and developing countries should be facilitated.
- Compatibility should be fostered through the use of common nomenclature, and, where possible, the pooling of databases should be encouraged.

HUGO (2002)

VI. Intellectual Property

- Human Genome Organisation (HUGO), *Statement on Patenting Issues Related to Early Release of Raw Sequence Data*, 1997.
- Human Genome Organization (HUGO), *Statement on Human Genomic Databases*, London, December 2002.
- Art. 29 Data Protection Working Party, *Working document on data protection issues related to intellectual property rights*, 2005.
- UK Biobank, *Policy on intellectual property (IP) and access*, 2005.

VI. Intellectual Property

- HUGO expresses the hope that the free availability of raw sequence data, although forming part of the relevant state of the art, will not unduly prevent the protection of genes as new drug targets, which is essential for securing adequate high risk investments in biology, and will not result in a shift of activities of the pharmaceutical industry to searching for compounds that give marginal advantages against known targets rather than taking risks with new targets.

HUGO, 1997

VI. Intellectual Property

Recommendations

1. Human genomic databases are global public goods.
   a. Knowledge useful to human health belongs to humanity.
   b. Human genomic databases are a public resource.
   c. All humans should share in and have access to the benefits of databases.

HUGO, 2002

VI. Intellectual Property

Access to samples for analysis

- UK Biobank will only physically release samples to researchers for analysis where a compelling case can be made to justify this.

  Normally, when an application is approved, UK Biobank or, more likely, a laboratory contracted by it, will undertake the analysis.

  Where the analysis involves a test that is proprietary to the user concerned, arrangements will be put in place to maintain confidentiality or otherwise protect the IP involved. A Sample Analysis Fee will be payable[…].

UK Biobank, 2005

VII. Benefit Sharing

- HUGO, *Statement on the Principled Conduct of Genetic Research*, 1996.
- UNESCO, *Universal Declaration on the Human Genome and Human Rights*, 1997.
- HUGO, *Statement on Benefit Sharing*, 2000.
- UNESCO, *International Declaration on Human Genetic Data*, 2003.

VII. Benefit Sharing

Article 12

- a) Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual
- b) The applications of research, including applications in biology, genetics and medicine, concerning the human genome, shall seek to offer relief from suffering and improve the health of individuals and humankind as a whole.

UNESCO, 1997

VII. Benefit Sharing

- Prior consultation with individuals and communities and their involvement and participation in the research design is a preliminary basis for the future distribution of benefit and may be considered a benefit in itself. Such prior discussion should include consideration of affordability and accessibility of eventual therapy, and preventive and diagnostic products of research.

HUGO, 2000

VII. Benefit Sharing

Article 19: Sharing of benefits

[B]enefits may take any of the following forms:

(i) special assistance to the persons and groups that have taken part in the research;

(ii) access to medical care;

(iii) provision of new diagnostics, facilities for new treatments or drugs stemming from the research;

(iv) support for health services;

(v) capacity-building facilities for research purposes;

(vi) development and strengthening of the capacity of developing countries to collect and process human genetic data, taking into consideration their specific problems;

UNESCO, 2003

A. Conclusion: Public Population Project in Genomics (P3G)

- The P3G international consortium is an initiative that goes beyond national population genomics projects.

  It has been launched in order to provide the international population genomics community with the resources, tools and know-how to facilitate data management for improved methods of knowledge transfer and sharing.

  Its main objective consists of the creation of an open, public and accessible knowledge toolbox.

B. Conclusion

Barriers ?

- Political
- Socio-ethical
- "Real" perceptions
- Consent

Necessary tools ?

- Semantic interoperability
- Explicit guidelines (Bermuda principles?)
- Appropriate ethical framework
- Appropriate level of ethics review.