

EBI – EMBL genotype to phenotype workshop

Wellcome Trusst genome Campus, Hinxton, UK, June 10, 2009

Ethical issues in genotype to phenotype domain



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What's at stake?

SNP

Science New Possibilities

LD

SNP

Society Negative Perception

“...the rapid pace of change has produced two powerful, but conflicting, social reactions. On the one hand, there is very strong public support for breakthroughs promising better medical diagnosis and treatments...; on the other, there are anxieties about increased loss of privacy and the potential for genetic discrimination, as well as about the capacity to regulate genetic science in the public interest.”

Essentially Yours: The Protection of Human Genetic Information in Australia, Australian Law Reform Commission, 2003.

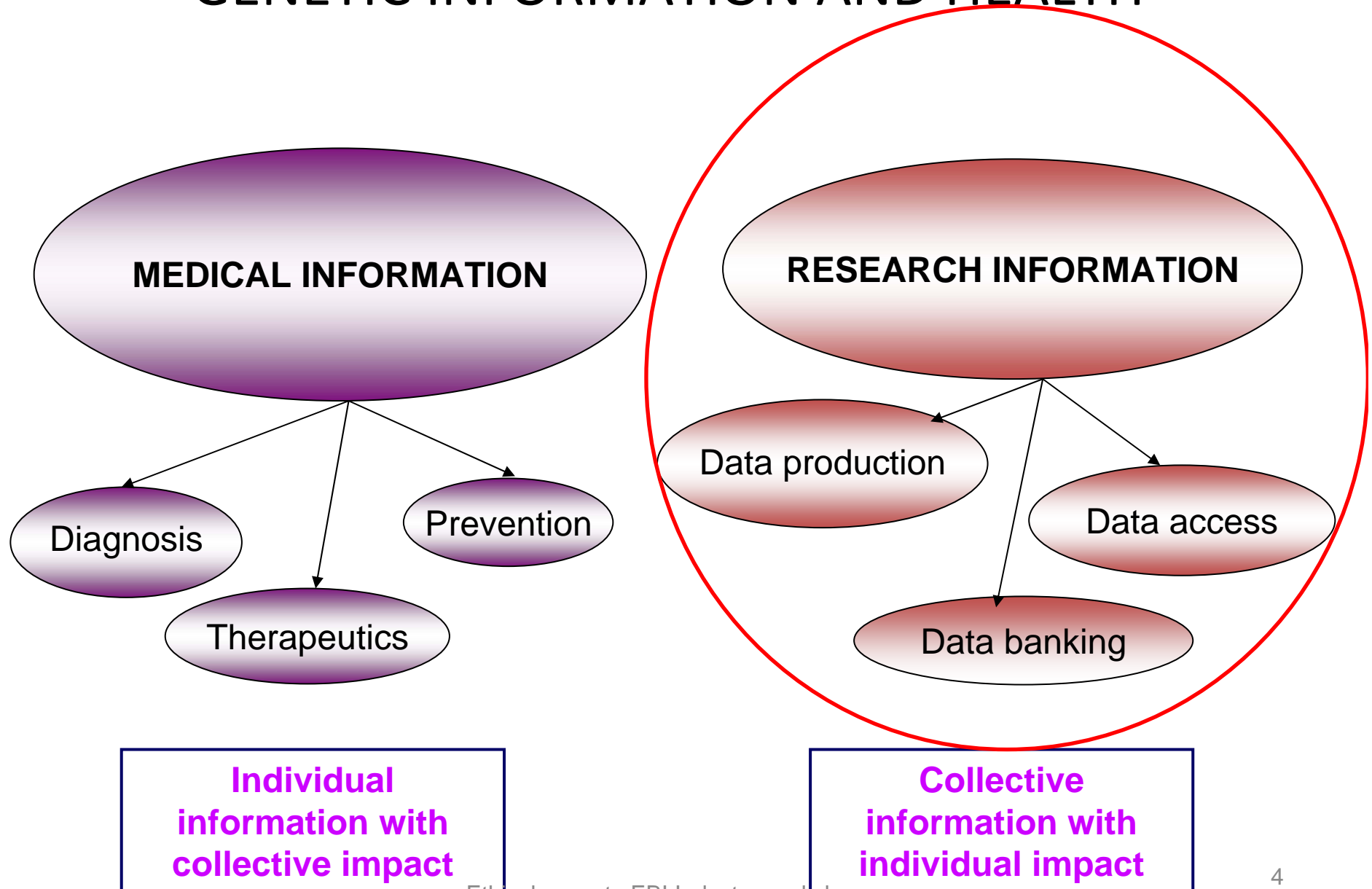
Specific questions

- Is large scale biobanking and whole genome analysis modifying the ethics landscape?
- Is accumulating various kinds of data interconnected transforming the questions?
- Is ethics promoting or preventing sharing of bioresources and data?



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GENETIC INFORMATION AND HEALTH



What do we need?

- Principles
- Instruments
- Tools
- Governance

Guiding principles

- Human dignity
- Human rights and fundamental freedoms
- Autonomy
- Privacy
- Non-discrimination and non-stigmatization

But also

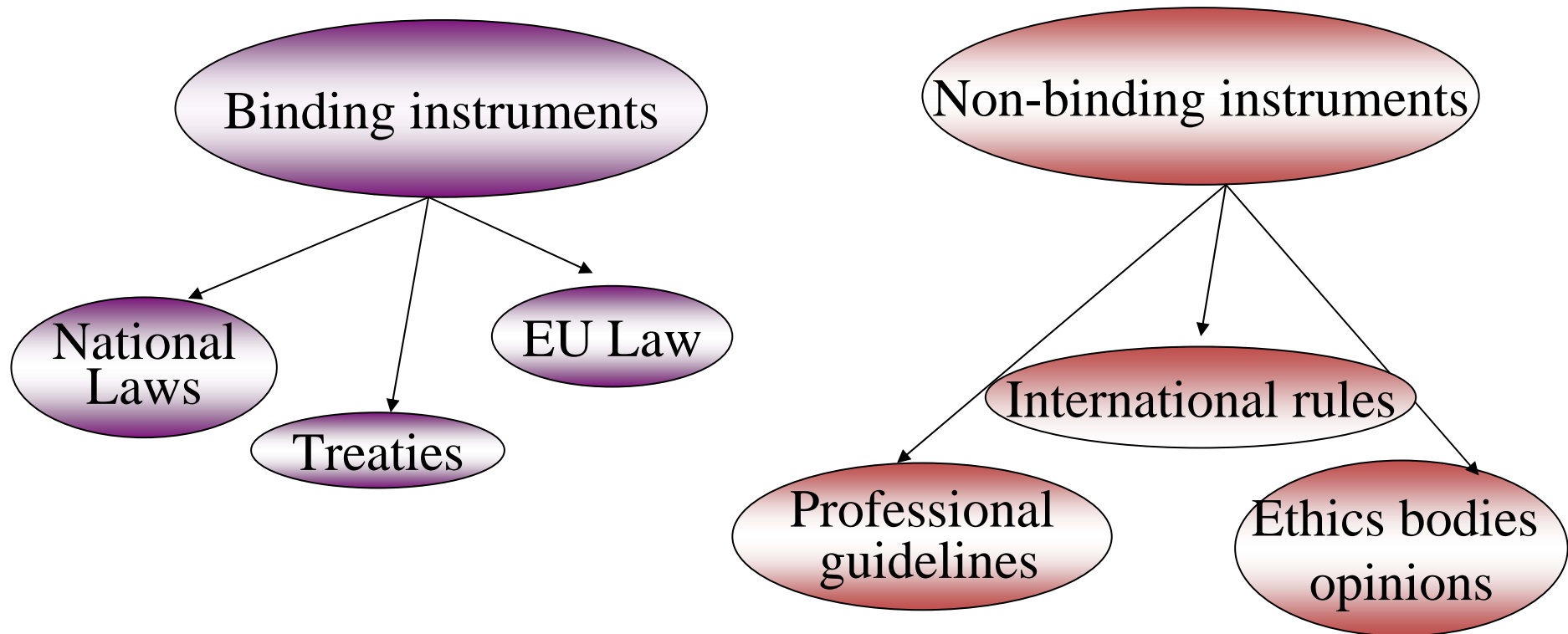
- Solidarity
- Common good



Duty to use, duty to share

versus intellectual property and desire of control

Levels of regulation framework applying to research genomic information production and use



Universal Declaration on the Human Genome and Human Rights, UNESCO, 1997.

- Need to address ethical issues of genetics (preamble)
- Genome – common heritage of humanity (art. 1)
- Respect individuals' uniqueness and diversity (art. 2)
- Non-commodification of the human genome (art. 4)
- Benefit-sharing (art. 12)
- Freedom of research (art. 12)
- Solidarity (art. 17)
- International co-operation (arts. 18, 19)
- The Universal Declaration is a starting point; it is now up to the States to put the Declaration into practice...

Practical application of an ethical framework

- Informed consent** (autonomy, trust)
- Independent ethics committee** (transparency + responsibility)
- Data protection and public release** (privacy, confidentiality)
- Rules of access** (transparency, justice)
- Data/sample sharing** (responsibility)
- Relevance of the degree of **identification** and control by the individual sample donor (respect of persons, non stigmatisation/discrimination)
- Ownership and return of results** (non commercial use of body elements, accountability, justice)

Some of the issues

- Right to know and not to know
- Return of results (research) and delivery of information (health care)
- Protection of confidentiality
- Production of mass genetic information
- Sharing of research data and results
- Research and clinical care sometimes mixed up

(a) Right to know

“No one should be denied access to his own genetic data...”

UNESCO (2003) art. 13.

“Personally identifiable information ... should be subject to adequate subject access rights”

WHO (2003) rec. 18.

“...after the completion of the study, subjects will be informed of the finding of the research in general, and individual subjects will be informed of any finding that relates to their particular health status”

CIOMS (2002) Guideline 5(7).

Right not to know

“... the person concerned has the right to decide whether or not to be informed of the results”

UNESCO (2003) art. 10.

“Adequate account must be taken of the privacy interest that individuals have in not knowing information about themselves.”

WHO (2003) rec. 16.

Balancing values evolve

“Ethics does not consist of a static set of theories or principles that can unproblematically be ‘applied’ to new situations.”

Knoppers and Chadwick, Nat Rev Genet, 2005

“However, informed consent is far from being a magical solution to ethical preoccupations,...”

Cambon-Thomsen, Nat rev Genet, 2004

“A focus on informed consent is also highly convenient for researchers and their institutions, and above all commercial enterprises. The reason is simple: insofar as individual rights delimit the domain of ethics, they shield other substantive issues from critical scrutiny.”

Garrath, Genomics, Society, Policy, 2005

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Controversial and evolving ethical issues

- Informed consent - (withdrawal, secondary uses)
- Confidentiality - (degree of identifiability; selection/discrimination - issues in use of genetic testing)
- Sharing of data and results - (the right to know and not to know, general vs individual results, public release, incidental findings)

Cambon-Thomsen *et al.* Trends in ethical and legal frameworks for the use of human biobanks. *Eur Respir J* 2007 ; 30 : 373-382

Genomics new ethical challenges

- Classical medical ethics principles mainly oriented towards individual protection
- Influenced by the paradigm of monogenic diseases
- Change of scale is triggering new questions also in ethical aspects.

Illustration through examples of biobank setting and use

Cambon-Thomsen A. The social and ethical issues of post-genomic human biobanks *Nature Reviews Genetics*, 2004 5: 866-873

Ethical issues in genome screen approaches

- Numerous markers might immediately or later on, in case of long term analyses, reveal information on other conditions than those that are the object of the study : issue of incidental findings and public release become major.
 - How to handle such potential information must be foreseen.
- Issues of re-identification and impact on data release policy
- Sharing of data and samples

General framework in France

- Legal measures for:
 - Protection of persons participating in medical research
 - CPP (Committee for protection of persons, equivalent REC)
 - Insurance
 - Informed consent (for secondary use, information + possibility of opting out = non opposition; but if full sequencing?)
 - Data protection authorities : Committee for approval of data treatment + specific committee for health related research – same level of protection in country of data origin/destination
 - Data protection in Europe (a directive)
 - Declaration (or authorization) for biobanks setting, conservation, use, transfer
 - Authorization for import/export of biological human samples

Challenging issues

- Full sequence, whole genome scan : as usual « test » or different?
 - For the moment nothing special for this case in France; discussions in the framework of a revision of law on bioethics and of law on biomedical research
 - Envisaged : more stakeholder, patients consultation
- No national policy for public data release: can be done if fully anonymized ; but?
- Incidental findings at large scale (so far, case by case, by study)

New developments, new issues

- Research developments challenge the existing frameworks
 - GWAS and Whole genome studies
 - Caulfield T et al.. *Research ethics recommendations for whole-genome research: consensus statement*. PLoS Biol. 2008 Mar 25;6(3):e73.
 - Specific issues :
 - consent,
 - withdrawal from research,
 - return of research results,
 - sharing & public data release

Issues of the future (1)

- **Duty to Recontact:**
 - Who, if anyone, has the duty to return results? Is there a “chain of obligation”
- **Right to Withdraw**
 - degree to which there is an ethical requirement to structure the research and dissemination of results in a manner that will allow the right to withdraw to endure as long as possible

Issues of future (2)

- **Risk/Benefit Analysis**
 - need for a comprehensive risk/benefit analysis of public data sharing
- **Governance Structures**
 - need to systematically evaluate existing and emerging governance structures

International collaboration

“...The full benefits for which the subjects gave their samples will be realized through maximizing collaborative high quality research. Therefore there is an ethical imperative to promote access and exchange of information.”

Data Storage and DNA Banking for Biomedical Research: Technical, Social and Ethical Issues, ESHG, 2001, art. 17.

What does prevent sharing of bioresources ?

Technical aspects?

Protection of individuals?

Intellectual / institutional protection?

Lack of rewarding mechanisms?

An example of recent questioning

- The open policy for sharing data challenged by new situations due to technological development in the domain of bioinformatics.

GWAS data sharing policy challenged by scientific advances

- A research team developed *a new bioinformatics method that allows the detection of a single person's SNP profile in a mixture of 1,000 or more individual DNA samples*
- *Homer et al., PLoS Genet 2008 4(8): e1000167.*
“Resolving Individuals Contributing Trace Amounts of DNA to Highly Complex Mixtures Using High-Density SNP Genotyping Microarrays.”
- In other words, bioinformatics techniques have progressed to the point that with enough genomic data on an individual from another source, it is now possible to determine whether that individual participated in a study by analyzing only the pooled summary data.

Adaptation

- This discovery has important policy implications for the way the scientific community shares such pooled sets of genetic data.
- Because individual SNP profiles can now be detected within aggregated data, controlled access to pooled datasets has become necessary.
- NIH, Wellcome trust, an EU project : GEN2PHEN

The general issue = combination of datasets may change the nature of the possible usages and the degree of identifiability

Present trends in biobanks/databases ethics

General framework tends to underline:

- The right to be informed and to exert a certain control on what is being done, even in case of anonymisation and minimum risk
- Many questions on the individual consent, but this is so far a very strong element
- The role of research ethics committees to assess whether or not a new consent is necessary
- But ethics Committees for research are still local and multiple permissions are being asked for in large consortium

What do we need?

- Principles
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Human Samples Exchange Regulation Navigator (hSERN)

- Allows addressing practically a series of relevant requests, for different countries, on the issue of regulatory aspects of exchanging human biological samples across borders.
- This web based tool is under construction and validation steps (not yet publicly open)
- It will permit to get information on validated theoretical as well practical legal aspects, for exchanges of human biological samples for research purposes.



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Sample Exchange Regulation Navigator

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Login :

Password :

[New Account](#)

SEND SAMPLE FROM FRANCE TO UNITED KINGDOM :

FROM FRANCE :

- [Overview](#)
- [Theory](#)
- [Practice](#)
- [Problems](#)

TO UNITED KINGDOM :

- [Overview](#)
- [Theory](#)
- [Practice](#)
- [Problems](#)

FROM FRANCE :

OVERVIEW

France has a specific framework to organise import/export of human biological samples for research. It consists of law and other regulations. They indicate the French agency delivering an authorisation and the different requirements to be fulfilled.

THEORY

To exchange tissues, cells and their elements including DNA (except stem cells of foetal or embryonic origin)

How I see the future

- Longitudinal monitoring of ethical issues rather than « approval and let's go »



Solid governance structures

- More implication of scientists in multidisciplinary societal activities
- More public consultation and more public involvement in policy making
- More transparency, dialogue, awareness
- Less scientific hype, less ethics « arrogance »

Some European initiatives regarding genetic information/genetic testing (1)

- Council of Europe:
 - Oviedo Convention on human rights and biomedicine (1997)
 - Additional protocol: Genetic Testing for Health Purposes (2008)
- European Union: EU law +
 - Council recommendation on a European action in the field of rare diseases (voted by EU parliament, April 23 2009)
 - European Group on Ethics of Science and New Technologies (EGE):
 - Opinion 6 of the EGE, 1996, on Prenatal Diagnosis
 - Opinion 18 of the EGE, 2003, on Genetic testing in work place
 - Statement 2003, on "Advertising genetic tests via the Internet"

Some European initiatives regarding genetic information/genetic testing (2)

- Report and 25 recommendations on ELSA of genetic testing by an expert group (2004)

http://europa.eu.int/comm/research/conferences/2004/genetic/index_en.html

- EUROGENTEST <http://www.eurogentest.org/>
- GMP to GBP : from good manufactorial practices to good bioethical practices (FP6, France biotech coordinator: guidelines http://www.france-biotech.org/TEMPLATES/TemplateGenerique.Asp?ID_DOC=4125)
- Presently a number of other projects are on track

Societal dimensions of genomics in EU R&D framework programmes

- The European Union (EU) has formally included four kinds of approaches:
 - a first mandatory modality is to consider ethical aspects in the management of projects ; specific panels review those aspects;
 - a 2nd one is to include them as part of the research work, as an identified research task in genomics projects;
 - a 3rd one is a specific line of research or coordination actions in “science and society”, (now “science in society”) with specific funding, where genomics is one among other topics;
 - a 4th one is within the EU R&D in social sciences and humanities where part of the calls make a place for genomics related issues.

Conclusion

- Not only science is challenging ethics but also ethics is influencing scientific choices and research design
- Involvement of the public in such choices is a challenge for scientists as well as for ethics committees
- Integration of all aspects in multidisciplinary projects or settings is an academic and human challenge.

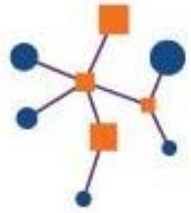
Biobanks, Genomics and public health

- The Inserm U 558 team: “Genomics and public health” has built the capacity to work interdisciplinary on those issues and has built an expertise and an international network, that has led to now offer services through a “societal platform”.

<http://societal.genotoul.fr/>



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