

HUMAN BIO-COLLECTIONS: Who Benefits from Gene Banking?



Briefing Number 14
April 2001

Whilst the publication of the draft human genome has been likened to the 'invention of the wheel' and the 'book of man', we still do not know exactly how many human genes there are or what makes humans genetically different from mice or even fruit flies (*genetic variation*). Nor does the map of the human genome tell us anything about how genes work - in relation to each other and in relation to the environment - or what genes actually do. In other words, it tells us nothing about *gene function*. Consequently, the publication of the human genome in particular has led to an escalation in the demand for genetic information so that vital questions about genetic variation and function can be addressed. Large collections of genetic material are therefore being established world-wide to facilitate research into, for example, links between specific genes and particular illnesses and how genetic variations between people affect susceptibility to specific diseases.

This briefing examines the case for such collections and focuses in particular on a current proposal by the Medical Research Council (MRC), Wellcome Trust and Department of Health (DOH) to establish a large population bio-collection in the UK. A number of crucial concerns are identified that must be addressed before this proposal is allowed to proceed.

What Are Human Bio-collections?

Human bio-collections consist of two or, increasingly, three components:

1. **Human tissue/fluid samples**, kept in cold storage, forming what is usually called a 'bio-bank'. Samples could include, for example, hair, blood, saliva, skin, semen, etc. (This is because human genetic information is replicated in every cell in the body and can be derived from any tissue or fluid containing cells.)

2. **Genetic data** that has been derived from analysing this biological material and then stored on computer, forming a genetic database.
3. **Personal records**, most usually *medical records* and *lifestyle data*. This aspect of human genetics collections is becoming increasingly prioritised and forms an important part of the proposed UK Population Biomedical Collection (see below).

What Are Bio-collections For?

Identifying People

Because (with the exception of identical twins) an individual's genome is unique to them, an obvious potential use of human genetics collections is as a mechanism for individual identification. Two existing examples of this use in the UK are the Police Forensic Database, set up with the aim of aiding the identification of offenders, and the Child Support Agency Database, used to test for paternity.

Medical and Psychological Research

Despite the fact that the Police Forensic Database is by far the largest bio-collection in the UK, most collections have been established to support research into how genes function in relation to the development of human disease and mental illness. The hope is to use data from human genetics collections to shed light on:

- the genes that cause diseases or might underlie susceptibility to diseases and mental illness (often called 'gene hunting' or 'mining');
- the nature of genetic variation between people (for example, in order that drugs might be tailored more closely to individual genetic profiles and adverse reactions avoided - an industry called pharmacogenetics);
- the complex ways in which genes interact with environmental factors in relation to disease and disease pathways.

Other Purposes

There are a range of other purposes for which human bio-collections could be used although the lack of a central register makes this difficult to document. Collections could, for example, be used for research into human evolution or for comparative studies between species. They could be used for purposes other than strictly medical – e.g. in research into slimming pills or other areas that begin to blur or cross the line between medicine and genetic ‘enhancement’. Similarly, collections could be used for work into behavioural genetics (research on the genetic basis of mental and behavioural processes).

Human bio-collections could be used for purposes that begin to blur or cross the line between medicine and genetic ‘enhancement’

The UK’s Proposed Population Collection

Most existing UK bio-collections – with the notable exception of the Police Forensic Database – have been set up to support discrete medical/psychological research projects¹. For example, the Avon Longitudinal Study of Parents and Children (ALSPAC) is following the development of children born to 14,500 women in Avon in the early 1990s and the Acute Coronary Event DNA Library (ADLIB) project has spawned a number of sub-projects all seeking to identify the “*genetic determinants of premature coronary artery disease*”. The MRC has also recently announced awards totalling £8.3 million to fourteen new bio-collections to study patients with particular diseases such as heart disease, diabetes and cancer and mental health problems².

In addition to such targeted collections, the publication of the first draft of the human genome has intensified a growing international trend towards establishing large scale and multi-purpose ‘population collections’ that incorporate genetic information alongside general lifestyle data and medical records. Some of the better known examples of recently established, and soon to be established, national projects include Estonia³, Iceland⁴, Sardinia⁵, Singapore⁶ and Tonga⁷. The hope is that, through their sheer scale, representativeness and ability to cross-reference biological, environmental and biographical data, such collections will have the potential to be used for a variety of research projects. As a result, the MRC and Wellcome Trust, in conjunction with the DOH, are currently proposing to establish such a collection – the UK Population Biomedical Collection (UK PBC) - in the UK^{8,9}.

The publication of the first draft of the human genome has intensified the trend towards establishing large scale and multi-purpose ‘population collections’

It is intended that the UK PBC would be partly publicly funded and would utilise the UK’s comprehensive stock of medical records. The aim would be to investigate disease, supposedly by looking for correlations between different diseases and genetic/environmental factors with a focus on genetic variation and gene-environment interaction. The MRC have pledged £20 million in principle to the project and further ‘millions’ have been promised by Wellcome¹⁰.

Consultations on the details of the proposal are still in progress but initial plans are to take samples and lifestyle information from 500,000 UK volunteers aged between 45-64. Genetic samples and lifestyle data would then be tagged with medical records and the information computerised and stored centrally for use by medical researchers. The project would be administered through GP surgeries in conjunction with specially established regional centres. It would be centrally managed and co-ordinated, with a separate body responsible to the public for overseeing the project as a whole. It is as yet unclear how access to the collection would operate, who would be given permission to use the data, or how such decisions would be made. No date has yet been announced for the launch of the collection.

Problems With The UK Human Bio-collection

The UK PBC will, if it goes ahead, involve a considerable financial commitment to genetics in this country. Bio-collections such as this clearly have the potential to provide valuable data for genetic researchers working in a range of settings, particularly medicine. However, there are a number of issues in relation to the current political and economic situation in the UK that will need to be addressed before we should contemplate establishing this project.

Problems with Data Quality

On a practical level, as lifestyle and medical information for the proposed UK PBC will presumably be collected prior to, and separately from, specific research projects which will use the data, it will be in severe danger of being too unfocused and superficial to be of any meaningful use. Even when a project has a clearly defined idea of the key pieces of information needed, obtaining lifestyle data of sufficient accuracy and detail is extremely costly, time-consuming and specialised. As Mike Pringle, Chair of the Royal College of General Practitioners, has pointed out, even attempting to establish a family history of genetic disease is not straightforward¹⁰. Patients will not necessarily be sure of the cause of a relative's death and a presumed father may not always be the biological father. Established collections such as ALSPAC conduct half day assessment sessions for each participant¹⁰ and it is unlikely that GPs will be similarly resourced to collect data for the proposed UK PBC. Even so, the strain on GP surgeries is likely to be considerable and, given the current financial crisis in the NHS and the severe strains on basic services, is this currently the best use of public money and resources?

There is a serious danger that data will be too unfocused and superficial to be of any meaningful use

Commercially Driven Research Agenda

In the last few years, commercial involvement in science has escalated. Genetics has been at the forefront of this blurring of the boundaries between public and private and most university genetics research projects are now part – if not wholly – funded by industry with economic, technological and scientific processes inextricably linked¹¹. Genetic information has become an extremely valuable commodity and a race is well underway to patent genes and gene sequences derived from tissue that has been freely donated¹² with claims for more than 127,000 human genes/gene sequences already filed¹³. Significant commercial involvement in medicine has brought commercial agendas to the fore and medical genetics in particular has become dominated by the short term interests of shareholders. In addition to the collections that are being established by the private sector itself (e.g. the American company DNA Sciences launched a web site appeal last August for public donations of DNA to develop its own bio-collection¹⁴), national population bio-collections are increasingly being established in conjunction with, or made available to, commercial companies. For example, exclusive rights to Tonga's new bio-collection have been sold to the private Australian company, Autogen Ltd⁷. In the case of Iceland, exclusive rights have been granted to the private company deCODE¹⁵, which has subsequently entered into a deal with the pharmaceutical giant Hoffman La Roche to allow it to commercialise deCODE's discoveries.

Medical genetics has become dominated by the short term interests of shareholders

Although the architects of the UK's proposed bio-collection have given public assurances that no similar 'exclusive rights' deals will be made with any one commercial company, it is currently unclear who will and will not be granted access to data from the collection. The current blurring of public and private boundaries within bioscience research means that commercial interests will inevitably feature in bids for access. Wellcome have also emphasised that they

consider the involvement of the British pharmaceutical industry “essential in the long run if we’re to get more targeted treatments or better medicines”¹⁶. Yet there is currently no co-ordinated attempt to address the implications of this commercialisation in bio-research. For example, a recent public consultation exercise by the Government’s new Human Genetics Commission on bio-collections failed to directly address this problem¹⁷.

Over-emphasis on Biology

Whether the focus is on finding genes which cause particular illnesses or genetic differences between people as these relate to disease, pressure to sell shares is likely to result in the increased framing of human health problems in purely biological terms (see Box 1) in the race to produce a new generation of ‘wonder drugs’. Current acknowledgements of the multi-causality of disease and the importance of understanding social, environmental and cultural factors¹⁸ seem unlikely to be incorporated into the design of genetics research agendas as there is no obvious financial profit to be gained from such an approach. Instead, multi-purpose bio-collections such as that proposed by Wellcome are likely to be increasingly used as ‘fishing ponds’ for molecular targets for drugs.

Threats to Human Rights

It is vital that the process of collecting genetic data and studies based on this data are conceived and managed in a way that fairly represents the interests of all sectors of the societies involved. Yet, again, whilst commercial interests remain unchecked it is unlikely that this will be the case. For example, accusations have recently been made that American researchers funded by the US company Millennium Pharmaceuticals and the American National Institutes of Health carried out genetic research in China without obtaining proper informed consent from the participants. It is also alleged that there was possible coercion and that participation made subjects subsequently vulnerable to discrimination and the possibility of sterilisation. Gwendolyn Zahner, the psychiatric epidemiologist who filed a complaint against the researchers, has said that: “Cheaper, larger, and faster genetics studies are possible in China only because the country has not yet established the legal, environmental, workplace, and medical protections afforded to American citizens”²¹.

Research projects that focus on perceived genetic differences between people as these relate to supposed mental or behavioural differences pose a particular threat to human rights and need to be especially closely scrutinised for potential abuses by vested interests. The focus on difference can often mask a more insidious process whereby one group of people tries to make behavioural or mental comparisons with another group in order to claim superiority. For instance, at the turn of the century, some scientists attempted to use a biological argument to defend the law which prohibited women from voting. Based on the observation that women’s brains are on average smaller than men’s, they argued that this made them less intelligent than men and, therefore, not intellectually capable of voting.

In the field of genetics research, apparent ‘discoveries’ of these types of oversimplified links are already prevalent. For example, researchers working on the Icelandic population database claim that they have identified a number of genes thought to cause the psychiatric condition known as schizophrenia²². Yet there is considerable evidence from the mental health literature that ‘schizophrenia’ is a label that describes a complex mental condition that may or may not involve a genetic defect as part of the overall picture. Other factors –

Pressure to sell shares is likely to result in the increased framing of human health problems in purely biological terms

The focus on difference can often mask a more insidious process

Box 1: Reductionism in Genetic Research

There are very few human diseases that can be directly attributed to a fault in a particular gene and even with these single gene disorders, patients with exactly the same genetic defect can range from extremely sick to mildly ill to completely healthy¹⁰. Environmental, social and cultural factors are therefore likely to be extremely important in determining the cause of their illness¹⁹. However, genetic research is increasingly framed in narrow biological terms (e.g. in relation to work on diabetes, heart disease, mental illness and obesity). For example, a recent article in Nature Biotechnology on obesity acknowledges that: *“In the past few decades, technological innovations have created a society where most forms of work are lighter, travel less strenuous, and lifestyles more sedentary. Add to this the overconsumption of food, in particular high-fat convenience foods, and you have the perfect recipe for a ballooning public health problem – obesity.”*²⁰ However, the remainder of the article is devoted to reviewing developments in the mushrooming field of biotech research dedicated to developing drugs that can intervene at the genetic level to adjust the body’s ‘weight control system’. The problem of obesity is therefore reduced to a problem of lack of medical understanding of how body weight is controlled.

Such a narrow biological focus ignores broader social factors and an overall impression is created that diseases and conditions such as obesity are caused by faulty genes. This perspective can be understood in economic terms as the financial incentive is obvious – there is a possibility of producing a highly marketable product. However, because the ‘quick techno-fix’ products from genetic research do not address the broader social and lifestyle factors involved in obesity, they are ultimately likely to be ineffective and even harmful in some cases (e.g. see the case of the withdrawal of the slimming drug Redux in 1996²⁰).

In a further example of the potential dangers of an over-emphasis on a ‘biological fix’ to a complex medical problem, Klaus Lindpaintner of Roche Genetics recently stated - in relation to a claim to have found a gene that might ‘cause’ schizophrenia (see section on *Threats to Human Rights*) - that: *“the gene just found could be used to identify family members most at risk before they fell ill, allowing doctors to target the minimum number of people with new drugs which delay or prevent onset of the disease”*²². Anti-schizophrenic drugs have had a somewhat chequered history in terms of the adverse effects they have been known to produce in the past (e.g. tardive dyskinesia). As Sue Baker of the mental health charity MIND puts it: *“There might be people who know they have a good chance of getting schizophrenia in future. Must they then spend the next 40 years taking drugs which make them ill in a different way?”*²².

notably the stress of being subjected to sustained racism – have been linked to the development of mental illness generally. Diagnosis of schizophrenia is notoriously difficult with a considerable margin for error and prejudice in clinical judgement. In addition, in the UK, Afro-Caribbean people are disproportionately more at risk of being detained by the police or the courts under the Mental Health Act and diagnosed as schizophrenic than any other group, leading some to argue that the label operates as a mechanism of social control.

As very little is yet known about gene function, there is actually very little that we can currently say with any certainty about the role of genes in mental processes such as schizophrenia. Moreover, the complexity of mental and behavioural processes - coupled with the subtleties of gene-environment interaction - mean that simplistic links between such conditions and one or several genes are inaccurate and potentially dangerous. This is because such oversimplified links can fuel discriminatory claims that one ethnic group may be somehow ‘mentally inferior’ to another and this, in turn, could lead to potentially oppressive practices against particular social groups.

There are very few human diseases that can be directly attributed to a fault in a particular gene

Oversimplified links between genes and mental health problems such as schizophrenia could lead to potentially oppressive practices against particular social groups

Without strict regulation and control, it is highly likely that human bio-collections could be used for a range of other purposes that stray even further from the medical sphere. These might include 'behavioural enhancement' - with all the oppressive connotations of eugenics practices in Nazi Germany - or the development of biological weapons which affect only those people with a particular genetic makeup.

Bio-collections will comprise highly personal and sensitive information that is potentially open to abuse

Data Security and Patient Control over Uses

Even if authorised research using human genetics databases is undertaken with democratic aims, collections will comprise highly personal and sensitive information that is potentially open to abuse. Looking at the UK PBC proposal, unique DNA will be linked with biographical information which will be stored centrally on computer. Responsibility for ensuring the confidentiality of such data would therefore pass from the individual doctor-patient relationship to the State. Such data could easily be used to discriminate against an individual for insurance or employment purposes, for example, and the Government has already given its official seal of approval for insurance companies to use results from one genetic test (Huntington's disease)²³. There is therefore considerable cause for public concern over how this data will be held and the regulations that will be in place to prevent misuse. A number of issues need to be urgently addressed before the Wellcome proposal is implemented:

Informed Consent

Given the possibilities for abuse at both a social and individual level, it is vital that samples are only taken from people who have explicitly agreed to take part in genetics studies. They should also be fully informed of the way their sample will be used and the range of potential implications for them of having their samples used in this way. This also raises the issue of how repeat consent will be gained from participants if their data is used for different research projects in the future. In a recently publicised Canadian case, an ethnic community known as the Nuu-chah-nulth in British Columbia who gave consent for their samples to be used nearly 20 years ago have accused a British researcher of using these samples recently for different purposes without consent and have demanded their samples back²⁴.

Anonymity

Individuals have a right to have their identity protected if they participate in a study such as Wellcome's. However, given that an individual's DNA is unique to themselves, ensuring that a bio-collection entry is completely anonymous is technically impossible, particularly as DNA data will be linked with biographical data and medical records. Furthermore, biographical data will need to be more than a 'one-off snapshot' to be of real use. This means that follow-up checks will need to be undertaken with individuals and this will necessitate researchers knowing their identity. Anonymity will be further jeopardised by the need to gain repeat consent for each new study. Therefore, in reality, the issue becomes one of how safeguards can be implemented to prevent theft or error and the access of data by researchers or companies for purposes that may have discriminatory consequences.

Feedback

Decisions will need to be made about whether - and how - relevant information that might arise from projects using human genetics collections should and could be fed back to the individuals concerned (for example, if researchers identified a genetic defect that the individual did not know about). At what point would a decision be made that the information was accurate and meaningful enough to be fed back to the individual? Who would give the feedback and

Given that an individual's DNA is unique to themselves, ensuring that a bio-collection entry is completely anonymous is technically impossible

would counselling be provided? What about an individual's right *not* to know? If information from an individual's sample has implications for other members of their family, should this be communicated to all those concerned even if they have not participated in the study? Does turning the project into a feedback model increase the possibility that anonymity will be breached and that the project could turn into a divisive screening programme? All of these questions need to be debated publicly before Wellcome's proposed bio-collection is implemented.

Lack of Effective Legal and Regulatory Framework

Human tissue for research has traditionally been viewed as either 'gifted' - where the donor signs a consent effectively giving the material away for unspecified research purposes - or 'abandoned', where tissue is simply taken for research after surgery or post-mortem. However, there is currently no effective legal or regulatory framework in the UK for controlling the collection and use of genetic material and there is no ban on genetic discrimination, e.g. by insurance companies or employers. There is also a lack of clarity in British law over whether anyone can actually *own* human tissue. Currently, human genetics collection holders tend to be defined by large organisations such as the MRC as 'custodians' in an attempt to circumvent this problem. Even so, despite the fact that they cannot claim to own the tissue itself, patenting law allows researchers to patent genetic information *arising from* tissue and to sell this information to others.

With regard to the actual use of human tissue for research, past and current practices in the UK have been regulated by the professions involved rather than Parliament. However, such a system will clearly not be able to cope with the demands of the new genetic technologies or gain public confidence, particularly as project funders, managers and regulators of collections can in practice be the same institutions. Furthermore, there are no specific guidelines in existence for population collections. The Office of the Information Commissioner (responsible for Data Protection) is only reactive and Regional Ethics Committees, which play a key role in granting permission for research projects to be carried out, will have no specific training or expertise in issues arising from human genetics collections²⁵. This is clearly an unacceptable situation and, as has been highlighted by the recent Alder Hey case, there is a significant danger that launching the UK PBC before establishing effective safeguards and controls is likely to lead to a public backlash.

Conclusion

Proposals for the UK Population Biomedical Collection are being drawn up at a time when there is considerable public concern about medical ethics and the issue of informed consent, particularly in the aftermath of the Alder Hey scandal. A recent MORI poll conducted for the Human Genetics Commission found that: *"Three-quarters of people feel they have too little information on controls on biological developments, and most have little or no confidence that rules and regulations are keeping pace with new scientific developments"*²⁶. Government proposed changes to legislation will go some way to improving the situation with regard to informed consent but many more issues will need to be addressed before allowing the collection to be implemented. An effective legal and regulatory framework must first be established in order to control the collection and use of genetic data to safeguard human rights and prohibit the misuse and abuse of this data. The potential for information to be used for discriminatory or other anti-democratic purposes in particular must be closely examined. A number of specific issues will urgently need to be addressed in

There is currently no effective legal or regulatory framework in the UK for controlling the collection and use of genetic material

Launching the UK Population Biomedical Collection before establishing effective safeguards and controls is likely to lead to a public backlash

this context in relation to the UK's rapidly expanding Police Forensic Database. The market driven rhetoric of genetic reductionism must also be dismantled if human genetics collections are to provide the raw material for medical research projects that will be of benefit to the public rather than to the shareholders of the companies involved. Finally, given the serious lack of resources within the NHS, the decision to commit considerable amounts of public money and GPs' time to the UK PBC should be a matter for public debate.

References

- 1 For examples of existing collections, see House of Lords Select Committee on Science and Technology – Written Evidence. Publications on the Internet. 6th November 2000.
<http://www.publications.parliament.uk/pa/ld199900/ldselect/ldsctech/115/115we01.htm>
- 2 The Medical Research Council announces funding for new genetic collections to study common diseases. MRC/65/00. 13th November 2000. http://www.mrc.ac.uk/whats_new/press_releases/PR_2000/mrc_65_00.html
- 3 Estonians give green light to gene bank. Nature 409: 127. 11th January 2001.
- 4 Iceland considers its genetic future. Nature Biotechnology 16: 896. October 1998.
- 5 Italy toasts Sardinia with SharDNA. Nature Biotechnology 18:1032. October 2000.
- 6 Singapore to create nationwide disease database. Nature 407: 935. 26th October 2000.
- 7 Biotech firm buys Tonga's gene pool. Adelaide Advertiser. 22nd November 2000.
- 8 See Wellcome Trust website: <http://www.wellcome.ac.uk>
- 9 See Martin, P. and Kaye, J. (1999) 'The use of biological sample collections and personal medical information in human genetics research'. Background paper for Wellcome Trust workshop on 'The collection of human biological samples for DNA and other analysis'. Wellcome Trust: London.
- 10 Coghlan, A. A wild gene chase. New Scientist 2268: 16-17. 9th December 2000.
- 11 Fransman, M. (2001) Designing Dolly: interactions between economics, technology and science and the evolution of hybrid institutions. Research Policy 30: 263-273.
- 12 Privatising knowledge, patenting genes: The race to control genetic information. GeneWatch Briefing No 11. June 2000.
- 13 Meek, J. Your life in their hands. The Guardian. 15th November 2000.
- 14 Boyce, N. Give us your genes. New Scientist 2251: 22. 12th August 2000.
- 15 Iceland's doctors rebuffed in health data. Nature 406: 819. 24th August 2000.
- 16 Wellcome News. Issue 24 Q3 2000 p 11.
- 17 Human Genetics Commission (2000) Whose hands on your genes? A discussion document on the storage, protection and use of personal genetic information. Human Genetics Commission: London.
- 18 See, for example, Dexter, M. The human genome: the present, the past, the future. Wellcome News Supplement Q1 2001 pp 2-3.
- 19 Weatherall, D.J. (2000) Single gene disorders or complex traits: lessons from the thalassaemias and other monogenic diseases. British Medical Journal 321: 1117-1120. 4th November.
- 20 Dove, A. Biotech weighs up the options in obesity. Nature Biotechnology 19: 25-28 January 2001, p25.
- 21 Harvard-affiliated gene studies in China face federal inquiry. The Boston Globe. 8th January 2000.
- 22 Gene find offers hope to mentally ill. The Guardian. October 21st 2000.
- 23 Share the risk. New Scientist 2261: 3. 21st October 2000.
- 24 Kleiner, K. Blood feud. New Scientist 2258: 7. 30th September 2000.
- 25 For a detailed discussion of these issues, see Kaye, J. and Martin, P. (2000) Safeguards for research using large scale DNA collections. British Medical Journal 321: 1146-1149.
- 26 Human Genetics Commission press release, 2nd March 2001.

GeneWatch



The Mill House, Manchester Road, Tideswell, Buxton, Derbyshire, SK17 8LN, UK
Phone: 01298 871898 Fax: 01298 872531 E-mail: mail@genewatch.org

Website and online database: <http://www.genewatch.org>

Subscribe to *GeneWatch*'s briefing series for news on genetic engineering developments.
For six issues: £12 individuals, £6 concessions (Europe £15, other overseas £20)
£100 businesses, £30 voluntary and educational organisations.