Genes on ice

As the UK's biobank begins its campaign to collect samples, **Geoff Watts** looks at what the banks do and the problems they raise

Some people call them genome databases; others prefer the term human genetic research databases. But if you want to raise their profile and catch public attention there is only one label that cuts the mustard: biobank. A more colourful word, it encompasses the notion of storage of biological samples for future reference.

Along with biological samples—collected principally as a source of DNA— these banks compile detailed personal information about their donors: what they do, how they live, and the illnesses they have.

Different banks have different aims.[1] Some are private, some public; some are large, some small; some try to reflect entire populations, while others concentrate on smaller subgroups. But the underlying intention in most cases is much the same: to reveal how genetic and non-genetic factors interact in determining health and disease, and then to exploit this knowledge.

The number of banks worldwide is uncertain. Isabel Fortier, an epidemiologist at the Montreal based Public Population Project in Genomics (P3G), tries to keep track of the international picture. She knows of around 70 that have 10 000 or more donors, and another 20 that are in the pipeline. Interest is growing worldwide, she says, in Asia as well as in Europe and North America.

How they work

A flavour of the biobanking enterprise can be gleaned from a handful of examples. One of the more ambitious schemes is UK Biobank, which began recruiting last week (www.ukbiobank.ac.uk). The intention is to gather information on the health and lifestyle of 500 000 volunteers aged between 40 and 69 years. Participants donate blood and urine samples, have basic health checks, and fill in a questionnaire.

"Over the next 20 to 30 years UK Biobank will allow fully approved researchers to use these resources to study the progression of illnesses such as cancer, heart disease, diabetes and Alzheimer's disease," declares a spokesperson for UK Biobank. The goals are new and better methods of prevention, diagnosis, and treatment. The scheme is funded by the Department of Health, the Medical Research Council, and the Wellcome Trust.

CARTaGENE, a Canadian biobank, was set up in 1999 (www.cartagene.qc.ca). It grew out of a collaboration between Quebec's four medical schools. It collects samples and data of much the same kind as its UK counterpart to explore the genetic diversity of its home province. Some 50 000 people aged 25 to 69 (roughly 1% of the population) will be recruited at random through Quebec's health insurance scheme. CARTaGENE is expected to run for at least 50 years.

The government of Estonia is a more recent entrant to biobanking. Legislation passed in 2001 set out plans for collecting samples and data from 100 000 people: a process that it (over-optimistically) hoped to have completed by the end of this year. The scheme was set up as a partnership between the government funded Estonian Genome Project Foundation and a company called EGeen. The company would have exploited any commercially valuable findings, with a proportion of the profits going to the foundation. The partnership was dissolved in December 2004 for undisclosed reasons,[2] but the scheme continues.

Of all the databanks, the Icelandic project has generated the most controversy. Like its Estonian counterpart it originated as a public-private partnership: between the government of Iceland and deCODE Genetics. The idea was to create a register of the entire Icelandic population comprising not only genetic and medical data but also genealogical records. This was to be licensed exclusively to deCODE for whatever medical use could be made of the information. The scheme was authorised by an act that passed the Icelandic parliament in 1998.

Individuals who objected to the scheme were to be allowed to opt out. But this didn't prevent critics from slating it as a government sell-off of citizens' data. After an outburst of public discussion, a court case in 2003 challenged the "presumed consent" approach. Iceland's supreme court ruled the act unconstitutional. The government declared its attention to introduce an amendment, but was overtaken by events when deCODE, undeterred by the setback, chose to proceed on a voluntary basis.

Thus far the company claims to have

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analysed the data from over 100 000 volunteers: more than half the adult population.[3] The results include the isolation of 15 genes and drug targets for 12 common diseases. Some drugs, including an antiplatelet compound for prevention of arterial thrombosis, are undergoing clinical tests.

Opposition

Whether private or public, most of these banking enterprises have had to face, or are still facing, complaints from various groups.[4] Poor design, insufficient discussion, inadequate prioritisation of resources, an over-emphasis on the role of inheritance, and the possibility of false positive results are just some of the criticisms. Even geneticists have had their doubts. In its early days UK Biobank was criticised by Sir Alec Jeffreys, a pioneer of some of the techniques of DNA analysis. He thought it would cost billions to get the required information and would generate many false positive leads. But his criticisms were based on a misunderstanding of the nature of the project, and he has since changed his mind.

In truth, it is not hard to understand why biobanks have often proved controversial. There are matters such as consent, confidentiality, and security that are familiar to researchers in all areas of biomedicine. When the work involves information with a predictive quality, and often with relevance to other family members, the public generally perceive the need for even tighter safeguards. While much medical research can be carried out on anonymous data, this is not the case with biobanks. The point of most studies is to consider genetic influences in parallel with medical and other life events, so samples and data must be reversibly anonymised. Biobanks generally go out of their way to emphasise that their arrangements meet and exceed minimum demands.

In any long running study in which it is impossible to predict what hypotheses the next generation of researchers may want to test, future use of material raises problems. One strategy is to consult every donor about each new project. Some banks have decided that this is impracticable and opted instead for a blanket form of permission. Donors do have a right to withdraw—though the conditions and caveats surrounding this "escape clause" differ from bank to bank. A related matter is the ownership of samples and data. Most biobanks seem to retain ownership—but, again, with varying conditions.

Equally diverse are the rules governing how the samples and data may be used. The core purpose of virtually all biobanks is medical research, but their material has all sorts of other potential applications from non-medical studies to catching criminals and establishing paternity. The Estonian Genes Research Act prohibits the forensic use of the bank's information; UK Biobank would make such information available only after a court order, which it might oppose. Here as elsewhere there is little uniformity of governance.

Then there is the question of whether to provide individual donors with information about their test results. UK Biobank supplies donors with details of their baseline measurements, but nothing more. The project, it argues, is a research study that makes no provision for the guidance and clinical back-up without which findings about an individual would be meaningless if not worrisome. At the other extreme is the Estonian project, in which participants have a right to request their genetic data.

Issues of intellectual property and the commercial exploitation of useful findings depend on whether the bank is a private or a public enterprise. In private banks the rights normally lie with the commercial sponsor, subject to any other arrangements that may have been made. In the case of publicly funded projects any profit is supposed to return to the bank itself or, in some way, to the community. That said, some banks' position on intellectual property betrays a surprising lack of forethought. Most biobanks make it clear to donors that they must not expect to benefit personally. But the more enlightened, appreciating that they owe their participants something in return, agree to keep them informed of any useful findings as these emerge.

Although most banks have their own ethics panel or other oversight bodies, international guidelines—such as those advocated by the World Health Organization5—have no binding force. In the absence of agreed protocols, wise banks will try to avoid future conflict by deciding in advance what they intend to do, and ensuring that all participants understand the rules of the game.

Speaking for P3G Dr Fortier declares her ambition for more collaboration. "Our major aim is to foster cooperation between different biobanks. The basic questionnaires are the same everywhere. Smoking, for example. Every study asks the question, but not in the same way, so it's not always possible to share the information."

Many of the larger biobanks are still relatively new and don't yet have much to offer in terms of results. "Some large and successful epidemiological studies are now going back to participants to collect blood, so they can add a genetics component," says Dr Fortier. Others that collected blood but were set up before the advent of the current generation of DNA technology are now exploiting it. In this category is the UK's highly regarded Avon Longitudinal Study of Parents and Children, set up to follow a cohort born at the beginning of the 1990s.

Not all biobanks succeed. An Australian scheme for studying the people of Tonga folded after just two years. And Boston University's hope of exploiting the records of the Framingham Heart Study came to grief in 2001 when it failed to reach agreement with its venture capitalist backers.[6]

Such setbacks make little impression on enthusiasts. The Nobel Prize winning molecular biologist Sydney Brenner spoke for many when he declared that the UK's scheme "will be the future of medical research."

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All references are on bmj.com