

Biobanks and translational research

Biobanks of samples donated by patients or the public are the cornerstone of the translational research/experimental medicine revolution that is taking place at present. In the UK many publicly or charitably funded clinical studies now routinely include the collection of blood or tissue samples as part of the study protocol to allow researchers to investigate important translational questions. For these same reasons, pharmaceutical and biotechnology companies are also collecting large numbers of such samples from participants in the multicentre and multinational clinical trials that they fund. An example of the usefulness of biosamples in translational research is the identification of a biomarker that is associated with, and can predict response to, a novel therapy – this is a very valuable asset for a pharmaceutical company and a very powerful tool for the clinician challenged with choosing the best therapeutic option.

Several local or institutional tissue banks have sprung up to support research by the staff of that institution and sometimes researchers from elsewhere can request access to these samples. Disease specific, or organ specific, banks, such as cancer and brain banks, are also gaining prominence, although some have been around for some time. Relatively new additions to the biobanking community are nationally coordinated large scale biobanks in the UK, and in a number of other countries, as strategic initiatives that aim to ensure that there are sufficient numbers of samples of consistent quality and obtained with consent that allows for future undefined research. In the UK, such national banks include the well publicised UK Biobank in the epidemiology arena and the Wales Cancer Bank and onCore UK in the oncology field.

The age of the biobank

Why all this biosample related activity? The reasons are multiple and collectively have brought human research biobanking to the fore. First, the scientific questions arising in the post-human genome sequence era require the investigation of biological variation between individuals and between diseases, drawing inferences from comparisons with the consensus human genome sequence. Examples of this are the “cancer-specific genomes” of the various subtypes of malignant neoplasm. Secondly, new enabling technologies allow the high throughput

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analysis of large numbers of human biosamples by the analytical techniques of the various “-omics”. Examples of these include expression analyses using genomics and proteomics, as well as metabolomics / metabonomics.

Enabling technologies are not restricted to those of laboratory analysis. Information technology is equally important to track and manage large scale sample archives, securely and anonymously label samples, correlate samples with complex clinical and pathological annotations, and link all of these with the masses of research data that can be generated from the samples.

In the UK, there is also another societal reason leading to a rebirth of biosample-based research. This might be regarded as the post-organ retention factor. There are new Human Tissue Acts in force in both Scotland and the rest of the UK, which have clarified the legislative framework in which biobanking takes place – even though this is a more regulated environment than before, it is probably better than that prevailing during the period of paralysis immediately following the events at Alder Hey, Bristol and elsewhere. Similarly, there are changes to how research ethics committees are run and to their approach to biobanking, with several research ethics committees specifically trained to consider the complex issues that biobanking raises.

Lastly, the funders of research are more willing than in recent decades to provide funding for facilitating infrastructure, as opposed to support for hypothesis-driven research projects. This is the main reason that several national biobanks, such as UK Biobank, onCore UK, the Wales Cancer Bank and others, have been funded in recent years.

Linked to the changes in the ethical-legal framework is the resurgence of interest from patients and the wider public to support

medical research by consenting to donate samples and information about themselves for biosample-based translational research. This is being reported by several banks and investigators, and indicates that the trust and confidence of patients has returned, if indeed it was ever really lost. Having gained trust, all of us involved in tissue banking now need to safeguard it and work with patients to ensure that their good intentions are realised.

The barriers to successful biobanking

If this is the “age of the biobank”, what are the practical problems in making them work? The first problem is the variation in opinions about the principles on which a research biobank should be run. For example, should sample banking *only* take place with patient consent? Should samples be provided to researchers free of charge or at a price? Should access be restricted to only local, regional or nationally-based researchers, or should it be more open? Should access be restricted to only researchers in the public sector, or also include those in industry? Whose interests come first – those of the researchers, the funders of the research, or the patients?

Many existing biobanks are run on models that are very much designed to favour the opinions and needs of those who founded or funded the bank, rather than on models reflecting a wider set of consensus views of many stakeholders. However, for the first time in the UK there is now a set of published *guiding principles* that have been recognised by a wide range of stakeholders. These are the guiding principles that were defined during the formation of the Confederation of Cancer Biobanks, a cooperative of existing cancer biobanks that has been formed under the auspices of the National Cancer Research Institute (see www.ncri.org.uk). These guiding principles recognise that consent underpins everything, and that it confers the trust of the donating patients on those involved in sample management and the sample journey to use in research. Flowing from consent, therefore, are the intertwined chains of trust, custodianship, supply and benefit. The guiding principles imply that actions by any individual along the chain, from the patient to the researcher, that hinders supply, acts possessively or denies the benefit being derived from the samples, inevitably also breaks the trust of the patient. These guiding principles, although written at a high level, are very useful touchstones for those involved in biosample collection, storage, transfer, or research. They outline the spirit to which policies and practices can be aligned. Further information can be obtained at <http://www.ncri.org.uk/default.asp?s=1&p=8&ss=4>.

The second problem is one of practicality. If banks are to be useful they need to create well-defined, controlled methods and standard operating procedures. Indeed, the fear that exists with many collections is that a study using such samples is as likely to find confounding variation between samples that reflects inconsistencies in sample taking, handling, processing, storage or characterisation, rather than true biological differences between samples and the patients from whom they were derived. Many banks employ some forms of quality control, but few employ any quality assurance, let alone a quality management framework. There are few recognised benchmarks for quality in research biobanking and the evidence base on which biobankers can build their choice of operating procedures is poor. As a result, different banks use, for example, different storage conditions/temperatures, different fixatives and processing methods, different approaches to sampling and QC, thereby making interoperability of samples from one bank with those of another very difficult. This has been recognised, in particular, by the US National Cancer Institute (which has made funding available for biobanking techniques research to help drive definition of sample quality) and by the European Commission (which has made large sums available via its Seventh Framework funding for consortia working to define quality, standards and norms in research biobanking). Lastly, an international consortium known as the Marble Arch International Working Group on Biobanking has been lobbying national and international standards

organisations for the creation of standards for certification and accreditation of research biobanks, as already exist for blood banks and collections of reference materials such as microbiological or cell culture types.

The third problem is that of resources. It will have become apparent to the readers that everything outlined above requires resources. The resources required are mostly human: people to take consent, to take samples, to process and stabilise/preserve samples, to collate annotating personal and clinical data, to define standard operating procedures, to manage quality, to ensure ethical and legal compliance, to manage relationships with patients, the public and other stakeholders, to facilitate access for researchers, and to provide leadership. However, not all the resources required are human; for example, other resources that have significant cost include premises to store samples, equipment, consumables such as containers, and information technology. As many research biobanking activities in the UK rely on pathologists in the NHS, there is a real challenge to identify the resources that exist, can be used in part for biobanking work, or need to be provided through special funding to ensure that this all works. The modernisation of pathology that is being considered at present by the Independent Review of Pathology team led by Lord Carter of Coles needs to remember that pathologists of all types have historically contributed a great deal to biomedical research, either through their own work or by facilitating that of others. In recent years this has sadly declined, but in the age of biobanking and translational research, rebuilding research capacity within the NHS pathology service to allow it to play its role in the national health research strategy is crucial. A good deal of this capacity rebuilding will be related to allowing pathology to play its part in biobanking and translational research.

The fourth is behaviour. Many pathologists show a great deal of goodwill towards tissue banking and buy-in to the spirit, but their involvement needs inevitably to be greater than goodwill alone. For biobanking to be successful, the active involvement of pathologists is needed. Pathologists may have to make intellectual contributions by helping in specimen handling and sampling to provide the portion for research. They may have to show leadership in their departments to adjust workflows to enable, for example, rapid handling of unfixed tissue to allow for snap-frozen samples to be taken. They may have to permit work to be carried out on their bench space, using their centrifuges or their microbiological safety cabinets, and they may have to convince their laboratory managers to allow biomedical scientists or laboratory assistants to use some of their time to facilitate sample handling. When it comes to converting willingness into action, the behavioural aspect comes into play. Pathologists may need to put aside the natural thoughts like, “Why should I?” “What’s in it for me?” “I’m not going to change my ways,” otherwise research biobanking will fail. Perhaps in the current climate of never-ending change, unfilled posts, squeezed budgets and the hangover of the organ retention period, this will be the most difficult challenge of all – what management consultants call the challenge of emotional alignment.

The last challenge relates to time. This is not the human resources time mentioned earlier, but rather the time related to the window of opportunity that exists during this age of the biobank. Scientists, policy-makers, funders of research and others are fickle. If biobankers and pathologists do not demonstrate that the investments and willingness to support biobanking for translational research can pay off by increasing research output, and ultimately by improving health, support will diminish, biobanks will close, scientists will move on to other models of biology and disease, and pathology will further lose its precarious foothold on research participation. Do pathologists really want to be relegated to the status of routine diagnostic “factory workers”? I don’t, and I doubt many of the readers do either. We came to this profession because it was inspiring, could make a difference to individuals in the clinics now and in the future through research, and was intellectually challenging. Let’s ensure that we embrace our roles in biobanking and translational research to keep these intentions alive.