Biobanking: the foundation of personalized medicine

Robert E. Hewitt

Executive Officer, European, Middle Eastern and African Society for Biopreservation and Biobanking (ESBB), www.esbb.org

Correspondence to Robert E. Hewitt, MB BS, PhD, 20 Boulevard du Roi René, 13100 Aix-en-Provence, France
E-mail: hewitt.r@sfr.fr

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Purpose of review

Biobanking has been identified as a key area for development in order to accelerate the discovery and development of new drugs. This review describes the recent advances in the field of biobanking and biospecimen research, with special reference to tumour banks which are the biobanks of primary interest in oncology.

Recent findings

There is a dramatic deficiency of high-quality, well annotated cancer biospecimens. Biospecimen research is a fast developing field that will improve biobanking methodology and biobanking is becoming more professionally organized with increased attention to quality management. Biobank networks are developing rapidly in order to combine and share resources.

Summary

Biobanking services must improve rapidly to serve the needs of personalized medicine and biospecimen research should be encouraged and supported at all levels from project funding to publication of results. Biobanks need to be run to high professional standards and the importance of adequate funding, training and certification must be emphasized. The growing presence of national and international biobank networks will allow biobanks to synergize. The development of a biobanking community will facilitate teamwork to overcome common challenges and enhance communication with multiple stakeholder groups.

Keywords

biobank, biospecimen, critical path, personalized medicine, tumour bank

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Introduction

In personalized medicine, therapies are selected for the individual patient based on the levels of different biomarkers in the patient's blood and tissues. Biobanks play a vital role here, because they provide the biospecimens required for research to identify useful biomarkers. There is growing hope that a focus on personalized medicine will speed up the translation of our rapidly increasing knowledge about disease processes into new and useful therapies. Problems with the old 'blockbuster' model of drug development were highlighted in a 2004 report from the US Food and Drug Administration (FDA) which found that: 'Today's revolution in biomedical science has raised new hope for the prevention, treatment, and cure of serious illnesses. However, there is growing concern that many of the new basic science discoveries made in recent years may not quickly yield more effective, more affordable, and safe medical products for patients. This is because the current medical product development path is becoming increasingly challenging, inefficient, and costly . . . Only a concerted effort to apply the new biomedical science to medical product development will succeed in modernizing the critical path' [1]. An area later identified for special attention by the FDA Critical Path Initiative was the development of better evaluation tools like biomarkers [2] and in subsequent recommendations from the AACR–FDA–NCI (AACR, American Association for Cancer Research; NCI, US National Cancer Institute) Cancer Biomarkers Collaborative group, emphasis was given to the need for improved biobanking services and biospecimen quality control [3••]. So improvement of biobanking services is high on the agenda for accelerating the introduction of personalized medicine, particularly in the area of cancer research. This review will chart recent developments in the biobanking field, focusing on those biobank types most relevant to the development of cancer therapies.

Biobank types

The term biobank has been defined in many ways [4] but the definition adopted here will be 'an organized collection of human biological material and associated information stored for one or more research purposes' [5]. Collections of nonhuman material (plant, animal, microbe, environmental) may also be described as biobanks but this is less relevant for the current review.

Biobanks of human samples fall into various categories, depending on purpose and design. They include disease-oriented biobanks, population-based biobanks and twin cohort studies [6,7]. Disease-oriented biobanks are most often hospital-based and include tumour banks as well as collections of blood and other samples from a variety of diseases together with normal controls [8•,9•]. In contrast, population-based biobanks are generally situated outside hospitals and the sample donors are normal volunteers, rather than patients. All of these biobank types are used for different kinds of biomarker research, so for example, studies on biomarkers of susceptibility require population biobanks, while studies on biomarkers of exposure or biomarkers of disease require disease-oriented biobanks [10]. They are also complementary, because individual research projects may require the support of more than one biobank type [6]. For example, if a study on disease pathogenesis leads to questions about disease aetiology, then samples (ideally cross-referenced) from both disease-oriented and population-based biobanks may be desirable. For this and other reasons the ongoing establishment of heterogeneous biobank networks like the BBMRI (Biobanking and Biomolecular Resources Research Infrastructure, http://www.bbmri.eu/index.php/home) network in Europe will increase research efficacy [6].

Tumour banks are the subset of biobanks of primary importance for studies on disease biomarkers in oncology and so tumour banks will be the main focus for this article. Like other hospital-based biobanks, tumour banks operate according to one or more of the collection models shown in Table 1 [11••].

Biospecimen quality

Biospecimen quality is a critical issue for tumour banks. The scale of the problem was revealed through The Cancer Genome Atlas (TGCA) project which had unexpected difficulty in sourcing adequate numbers of high-quality, well annotated biospecimens [12•]. This message and the need to upgrade research biobanking were communicated very effectively by a recent *Wired Magazine* article [13•]. Biospecimen quality is and has been a critical issue for all research studies utilizing biospecimens and this includes much of cancer research over the last 20 years [14•].

Key points

- Biobanking services must improve to supply the high quality, well annotated biospecimens needed for drug discovery and development.
- Biospecimen research is a growing field which is essential for improvement of biobanking services.
- Biobanks are becoming more professional with increased attention to quality management.
- Biobanks in the public sector need to collaborate with pharmaceutical companies for mutual benefit and must be sensitive to the wishes of donors and potential donors.
- Biobanks are forming national and international networks to share and combine resources.

Biospecimen research

Our knowledge of how to ensure biospecimen quality depends on biospecimen research, which until recently has been a rather neglected field. Effort is required to educate the scientific community on the merits of biospecimen research, to encourage funding agencies to support it and to encourage journals to publish it. Fortunately, progress is being made. The NCI's Office of Biobanking and Biospecimen Research (OBBR), founded in 2005, has raised the profile of this important discipline through initiatives like the Biospecimen Research Network Symposia [15•], and the Biospecimen Research Database [16•]. Another significant development has been the SPIDIA (Standardisation and improvement of generic Pre-analytical tools and procedures for In-vitro DIAgnostics, http://www.spidia.eu/) project, a 4-year project launched in 2009 and funded by the European Union to the value of 9 million Euros. This project is coordinated by QIAGEN GmbH which brings together a consortium of 16 leading academic institutions, international organizations and life sciences companies. The project aims to standardize and improve pre-analytical procedures for in-vitro diagnostic testing.

Currently, biospecimen quality is measured in a variety of ways. Histological analysis is important for tumours, to

Table 1 Three different biobank collection models

Model	Advantage	Disadvantage
Prospective collection model: samples are collected to meet the investigator's specific requirements	The investigator receives exactly what has been requested (e.g. specific sample processing requirements)	It may take months or years to collect enough samples especially if follow-up data are required
Banking model: samples of potential interest are collected and stored until needed	It may be possible to provide investigators with all the samples and data required immediately	The investigator may not receive exactly what is required
Clinical trial model: samples are collected from a clinical trial	Ideal if the parameters of the clinical trial are relevant to the investigator	The original consent may not allow secondary use

Many biobanks operate by a combination of these models [11••].

determine sample composition in terms of the proportion of tumour cells, normal cells, fibrosis, necrosis, inflammation and other characteristics. Involvement of a pathologist is essential for this assessment and should be encouraged in subsequent research [8•]. Quality criteria will depend on the study in question, so for example a sample with a low proportion of tumour cells may be unacceptable for expression profiling but adequate for PCR-based detection of genetic alterations. Molecular analysis is important for all types of biospecimen. DNA integrity is more important for some studies which may involve whole genome amplification, than for others involving real-time PCR for example [17•]. RNA integrity is critical for many studies and can be assessed by gel electrophoresis [18•]. Again, quality criteria will depend on the study in question and there is no single gold standard. The important issue is that samples must be 'fit for purpose'. Although RNA degradation may result from inefficient storage systems, it should be noted that changes in RNA expression pattern may be a more significant consequence of delayed sample processing [19•]. Analysis of many other molecular components may be important for quality control and there is a pressing need for biospecimen research to identify additional 'biomarkers of sample quality' [8•]. For situations in which adequate biomarkers of sample quality are not available, the best approach is to record all the pre-analytical variables that may affect sample quality, so that samples unlikely to be suitable for particular studies can be excluded. The SPREC (Sample PREanalytical Code) coding system has been developed to facilitate the recording of such information for each individual sample [20•]. One of the problems encountered in biospecimen research has been the difficulty in comparing studies because of their different experimental designs, so a standard protocol has been proposed to address this problem [21•]. New publication practices could also facilitate comparisons between studies if journals require authors to provide detailed information on biospecimen procurement and processing [22•]. This would also focus attention on the need to ensure high-quality biomaterials. If funding agencies demand that grant proposals provide similar information, this would also be helpful.

One pre-analytical variable of particular interest in tumour banking is the ischaemia time which, as noted above, affects the RNA expression profile. This includes the warm ischaemia time (from blood vessel ligation to surgical excision time) and the cold ischaemia time (from excision to freezing). Ideally, the length of both times should be kept to a minimum and both should be recorded [10]. Clearly this is more difficult for the warm ischaemia time which depends on a surgical procedure taking absolute priority. The cold ischaemia time is likely to be relatively less important, because stress-induced biochemical changes take place less rapidly at lower temperatures, but it should still be kept to a minimum. The acceptable limit for cold ischaemia time is currently a matter of debate [11••].

An untapped opportunity in biospecimen research is to draw on the experience of researchers in the closely related field of cryobiology [22•,23••]. Whereas biospecimen science focuses on the effect of pre-analytic variables on molecular components of a sample, cryobiologists are generally more interested in the effects of pre-analytic variables (including freezing) on the subsequent viability and functionality of recovered cells. Obviously, there is a lot of overlap and because cryobiology is not a new field, there is a wealth of experience to draw upon. Having said this, it should be noted that existing cryopreservation protocols are far from adequate [24••] and given the growing importance of cell therapy in medical care this is another field that demands urgent attention. This adds to the importance of collaborations between biospecimen scientists and cryobiologists in the more general area of 'biopreservation science'.

Best practices and quality management

In order to be efficient and reliable, biobanks must adopt and implement best practices, including policies and standard operating procedures (SOPs). A number of different organizations have produced best practice guidelines including ISBER (International Society for Biological and Environmental Repositories, http://www.isber.org), OBBR, IARC (International Agency for Research on Cancer, http://www.iarc.fr), OECD (Organisation for Economic Co-operation and Development, http://www.oecd.org), ABN (Australasian Biospecimen Network, http://www.abrn.net) and others. The three main themes tend to be technical best practices on infrastructure and specimen handling, recommendations on informatics and data management, and recommendations on ethical, legal and social issues [25••]. In addition to these guidelines, Molecular Medicine Ireland has published SOPs for biobanks which cover a wide range of procedures such as blood collection and DNA extraction from blood [18•] and their guidelines have been accepted as the first version of the BBMRI Laboratory manual [26•]. Other SOPs for biobanks are provided online by CTRNet (Canadian Tumour Repository Network, http://www.ctrnet.ca).

The harmonization of best practice policy guidelines and agreement on SOPs for laboratory procedures are a high priority, given the importance of international collaborations in research. SOPs must be evidence-based and will evolve as a result of advances in biospecimen research. Best practices and SOPs are also important in the area of clinical data collection. Here there is much to be gained by collaboration with hospital-based cancer registries which are highly professional, well regulated units within

many cancer centres (North American Association for Central Cancer Registries, http://www.naaccr.org; International Association of Cancer Registries, http://www.iacr.com.fr).

The Association Francaise de Normalisation (AFNOR, the French Standards Organisation, http://www.afnor.org) produced the first quality standard specific to biobanks in 2008. This is standard NF S 96-9000 and is based on OECD recommendations and the ISO 9001 : 2000 standard. So far no international norm exists that is specific for biobanks but the ISO 9001 : 2000 standard is relevant to many aspects of biobank management and is increasingly being adopted by biobanks in Europe. Additional standards are required by biobanks involved in assays and calibration (ISO 17025:2005) and production of reference material (ISO Guide 34:2000) [27]. The establishment of reference repositories with carefully characterized biospecimens for control and comparison purposes was one of the recommendations of the AACR–FDA–NCI Cancer Biomarkers Collaborative group [3••]. The formation of an international or preferably global authority to set and maintain standards and provide biobank accreditation is an important opportunity for the future [23••]. Such developments will not only raise standards, but also give biobanks the recognition they require as professional organizations. Another important priority is to establish training and certification schemes for biobank staff and further training for pathologists involved in biobank management [9•]. Providing a quality biobanking service obviously depends on quality staff but perhaps this fact requires extra emphasis.

Technology to promote quality

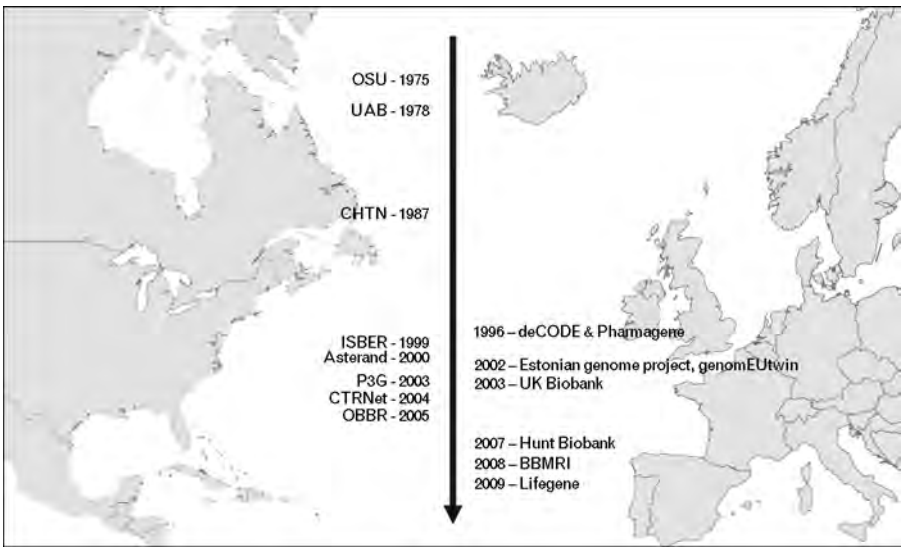
There are many ways in which technology can also help ensure biospecimen quality. As well as the obvious example of reliable freezers with monitoring and alarm systems, there are a variety of new technologies including ambient temperature storage solutions which are gaining acceptance (http://www.isber.org). The use of laboratory information management systems (LIMS) is also important for sample tracking and helping to ensure that SOPs are followed rigorously. Another important example of valuable new technology is automation, which has many advantages [12•]. Not only is automation labour-saving, but also it ensures that procedures are carried out in a highly standardized and reproducible manner which cannot be matched by a human operator. The disadvantage for medium-scale and small-scale biobanks is that automation tends to be expensive but prices will come down (http://www.isber.org).

Sample numbers and networks

Research studies require not only high-quality samples, but also adequate numbers of samples. The rarer the disease, or specific subtype of interest, the more difficult it is to provide large numbers of samples. It should be appreciated that tumour banks generally exist in hospitals and the number of samples that they can collect is restricted not only by the number of cancer cases seen per year, but also by factors like the diminishing size of cancers as a result of successful early detection through screening programmes. As a result, cancers are often too small to permit sampling for research. To increase the sample numbers available for research studies, tumour banks need to collaborate and pool their collections. This can be achieved by establishing central collections to which multiple tumour banks contribute. Another way is by formation of federated networks in which multiple tumour banks share a common online database and retain control of their collections, but agree to make collective contributions to meet investigator requests. The federated model has worked well for a number of tumour bank networks [28•]. Another interesting new approach is that of the 'Biolibrary', an organizational unit that focuses on acquisition, cataloguing and distribution of biospecimens, from multiple hospitals to multiple biobanks across a region. This model has been found to increase sample accessibility [29•].

The CHTN (Cooperative Human Tissue Network, http://www.chtn.nci.nih.gov) is an example of a large network including tumour banks across the USA. Experience gained in this 23-year-old network forms much of our knowledge base in the biobanking field (Fig. 1). In South Korea there is the KNRRC (Korean National Research Resource Center, http://www.knrrc.or.kr/english/index.jsp), founded in 1995, which is smaller (approximately 40 biobanks), but the organization of this very heterogeneous human/animal/plant/microbe biobank network and the synergy achieved provides an interesting example [30•]. The new BBMRI network in Europe is becoming a heterogeneous network of unprecedented scale, containing a variety of human biobank types, both population-based and disease-oriented [7,31•]. There is also an OECD initiative to establish a Global Biological Resource Centre Network (GBRCN) (http://www.gbrcn.org) and a pilot study is currently underway [7]. For such projects to be successful, the existence of shared standards and policy harmonization is vital, as emphasized particularly by P3G (Public Population Project in Genomics, http://www.p3g.org) [32]. The great synergistic potential of international biobank networks with scientific, medical and economic benefits provides a strong incentive for all the necessary preparations [6]. To promote communication between all the major international organizations involved in biobanking human samples, a think-tank or working group called the Forum for International Biobanking Organisations (FIBO) has been formed, with representation from BBMRI, IARC, ISBER, KNRRC,

Figure 1 Developments in biobanking in geographic and historical perspective



The figure shows the start dates of different biobanking initiatives on either side of the Atlantic. Ohio State University Tissue Procurement facility (OSU) and University of Alabama Tissue Collection and Banking Facility (UAB) were forerunners of the US Cooperative Human Tissue Network (CHTN). Pharmagene was a commercial biobank that provided samples and services to the pharmaceutical industry and it merged with Asterand in 2005. deCode, the Estonian Genome Project, UK Biobank, HUNT Biobank and LifeGene are all population-based biobanks and GenomeEUTwin is a twin cohort study. ISBER is a biobanking society and P3G is a not-for-profit international consortium that serves the international population genomics community, working with biobankers and other subject matter experts. CTRNet is the Canadian Tumour Repository Network and OBBR is a department within the US National Cancer Institute.

OBBR and P3G. FIBO acts as a communications forum for different biobanking organizations. It helps build trusting relationships between organizations, to identify common goals and areas for collaboration, to coordinate efforts and achieve synergy. It focuses on developing highquality biobank infrastructures and building the capacity of these resources to network and exchange data and material at the international level. Since its formation in Paris in December 2007, the FIBO group has met a total of seven times and discussions have contributed many of the ideas mentioned in this review.

Biobank sustainability

Running a professional biobank requires adequate staffing, including pathology support, a manager, technicians and consent personnel in addition to necessary equipment, and it is universally accepted by biobank managers that biobanks cannot be sustained by cost recovery alone [8•,9•,10]. Tumour bank sample collections take years to develop and more years to acquire follow-up clinical data. Well-motivated professional staff are required. Staff turnover can be very disruptive. Hence for an individual tumour bank, long-term institutional support is essential [8•]. As tumour banks join cooperative networks that extend nationally and internationally, individual efforts can be combined and challenges shared. Societies like ISBER provide a discussion forum and networking opportunities that encourage the development of a biobanking community. This can complement the efforts of international biobanking networks.

As stated in the 2004 FDA report, 'medical product development path is becoming increasingly challenging, inefficient, and costly' [1]. Part of the problem is that public sector biobanks and pharmaceutical companies have so far had limited success in working together. If this situation can be changed, biobanks will be able to attract the funding support that they need from pharmaceutical companies, the pharmaceutical companies will gain better access to the biospecimens that they need for the drug discovery and development, and patients will be provided with better drugs [33]. Obstacles in the way of this highly desirable 'win–win–win' solution include legal and ethical issues like intellectual property and concerns about commercial use of patient samples and data. Public support will be a key element of success in overcoming these obstacles, so public engagement by the biobanking community is essential. As a possible solution, BBMRI has proposed the concept of expert centres, in which pharmaceutical research would be conducted outside the industry setting, donor material would not move outside biobanking infrastructure, and industry would not have exclusive rights to data generated [33]. One additional obstacle to public-private partnerships is the lack of quality assurance in many public sector biobanks. Pharmaceutical companies need to be convinced that they will be provided with samples of

adequate quality. The certification and accreditation of biobanks will help overcome this problem.

Protecting the patient

For biobanks in general, protecting the donor against research risks is a key responsibility. The measures taken must also be considered satisfactory by potential donors, because unless potential donors are adequately reassured, biobanking initiatives can be seriously compromised, as happened in Iceland for example [34]. In biobanking and the associated noninterventional research, the risk to the patient is that personal data may fall into the wrong hands (e.g. insurance companies, employers, etc.), so data protection is a key issue. To put this risk in perspective as far as hospital-based biobanks are concerned, it should be remembered that fully identified patient data (personal, clinical and laboratory data) is routinely stored on hospital databases to support their medical care. Biobanks generally give exceptionally high priority to patient confidentiality and data protection. Different protective measures available include institutional review board (IRB) or ethics committee review of research projects requiring biospecimens, informed consent (which protects the patient's interests by respect for autonomy) and a range of technological data security measures. In addition, there are various legal protections relating to all of the above, which vary from one country to the next and which are in need of harmonization to facilitate international collaboration. One more item that can be added to this list is staff training and certification, to instil a responsible and professional attitude.

Recent trends in biobank ethics

In recent years, ethical debate in biobanking has focused especially on the validity of general or broad consent [4]. For example, some would argue that the more general the consent is, the less informed it becomes. Others would say that if the information provided covers all aspects relevant to the person's choice, then that person's consent is appropriately informed [35••]. Fortunately for those biobanks following the 'banking collection model' described earlier, a move towards broad consent for future research use is now regarded as the emerging trend in biobank ethics [4,35••]. Other encouraging news includes the fact that a consensus has emerged regarding the nomenclature and definitions for terms relating to the identifiability of samples. The existence of many different terms to describe different levels of identifiability, coupled with their many different interpretations, has posed a major problem for discussions on confidentiality issues. Now, a nomenclature proposed by the European Medicines Authority (EMEA) has been adopted by the International Conference on Harmonisation of Technical Requirements (ICH) which brings together the regulatory authorities of Europe, Japan and the USA [36]. Briefly the nomenclature is as follows: 'Identified' data and samples are labelled with personal identifiers such as name, or identification numbers (e.g. social security or national insurance number). 'Coded' data and samples are labelled with at least one specific code and do not carry any personal identifiers. 'Anonymized' data and samples are initially single or double coded but the link between the subjects' identifiers and the unique code(s) is subsequently deleted. Once the link has been deleted it is no longer possible to trace the data and samples back to individual subjects through the coding key(s). 'Anonymous' data and samples are never labelled with personal identifiers when originally collected, neither is a coding key generated. Therefore there is no potential to trace back genomic data and samples to individual subjects [36]. While consensus is finally developing in areas such as this, interesting and important new ideas are emerging in the field of biobanking ethics which are now the focus of active discussion and debate. For example, with the realization that absolute data safety is an illusion, the idea of 'open consent' has been proposed, which refrains from any promises of anonymity, privacy or confidentiality [37•]. Also, it has been argued that there is a 'communitarian turn' in ethical thinking, with a shift in emphasis away from the individual and autonomy, in the direction of the community, solidarity and citizenry [38]. It will be interesting to see where these developments lead.

Problems with informed consent

Meanwhile, attention needs to be paid to practical matters concerning implementation of informed consent for research use of residual tissue. Realistic working solutions need to be found. To obtain informed consent in a conscientious manner, it is generally necessary to counsel patients for periods of around 20 minutes. It is difficult to discuss all the items required for informed consent in a shorter period of time. The fact that in general patients are highly supportive of biobanking for research, does raise questions about the wisdom of requiring this lengthy counselling procedure in the tense preoperative period. Rates for informed consent are typically more than 90% and as evidence of the motivation of patients to support biobanking, many disease-based biobanks have actually been founded by patient groups [38]. Another issue is the difficulty and expense of obtaining informed consent from hospital patients. Patients waiting for surgery do not arrive conveniently at a study centre for consent and blood taking. Instead, they have to be found somewhere in the hospital system, at a time when they are available. All this consumes staff time and valuable research funds. There is a sense of frustration among many clinicians and tumour bankers that current consent requirements are not based on an understanding of the practical realities in a hospital setting [22•]. Not all tumour banks can afford to employ dedicated staff for consent taking, which means that the task can only be

carried out by cooperative nurses or hospital doctors whose primary concern is patient care. Postoperative informed consent is one practical solution that can make the consent process somewhat more efficient [39•], but the process is still time-consuming and expensive. Whatever practical solutions are developed, they must have popular support and so the public should be involved in discussing the possible options. Public engagement can be achieved by focus group discussions for example and online interactions on the Web [37•,38].

Conclusion

Biobanks (including tumour banks) must be professional organizations [9•]. Only then will they have the recognition and support that they need from their host institutions and stakeholders, only then will they be able to deliver the high-quality service that researchers require, and only then will they be able to give patients and donors the full protection that they deserve. Biobank managers need to be trained and certified professionals. Biobanks need to operate according to consensus best practices and be accredited by an international or global authority. Biobanks must be adequately funded. Biobanks must also have stakeholder support and listen carefully to the views of potential donors. We have a long way to go before we reach all these goals and as indicated by the previously mentioned FDA reports, we need to make rapid progress [1,2].

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 130).

1 U.S. Food and Drug Administration. Innovation or stagnation: challenge and opportunity on the critical path to new medical products. March 2004. http://www.fda.gov/downloads/ScienceResearch/Special-Topics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm113411.pdf. [Accessed 5 April 2010]

2 U.S. Department of Health and Social Services and U.S. Food and Drug Administration. Critical path opportunities report. March 2006. http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/default.htm.

3 •• Khleif SN, Doroshow JH, Hait WN. AACR–FDA–NCI Cancer Biomarkers Collaborative Consensus Report: advancing the use of biomarkers in cancer drug development. Clin Cancer Res 2010; 16:3299–3318.
This study recommends strategies to overcome existing barriers to the use of biomarkers in accelerating the identification and adoption of new therapies. Recommendations cover biospecimen quality control, analytic performance, standardization and harmonization, bioinformatics, collaboration and data sharing, regulatory issues, stakeholder education and communication and science policy.

4 Cambon-Thomsen A, Rial-Sebbag E, Knoppers BM. Trends in ethical and legal frameworks for the use of human biobanks. Eur Respir J 2007; 30:373–382.

5 Kauffmann F, Cambon-Thomsen A. Tracing biological collections: between books and clinical trials. JAMA 2008; 299:2316–2318.

6 Gottweis H, Zatloukal K. Biobank governance: trends and perspectives. Pathobiology 2007; 74:206–211.

7 Yuille M, van Ommen G-J, Brechot C, *et al.* Biobanking for Europe. Brief Bioinform 2008; 9:14–24.

8 • Bevilacqua G, Bosman F, Dassesse T. The role of the pathologist in tissue banking: European Consensus Expert Group Report. Virchows Arch 2010; 456:449–454.
This study provides recommendations for pathologists and the institutions hosting biobanks on how to better integrate and support biobanking activities.

9 • Hainaut P, Caboux E, Bevilacqua G, *et al.* Pathology as the cornerstone of human tissue banking: European Consensus Expert Group Report. Biopreserv Biobank 2009; 7:157–160.
This paper calls for increased recognition of the role of the pathologist in tissue banking and encourages their involvement as scientific contributors to research on biospecimens as well as professionalization of tissue banking.

10 Riegman PHJ, Morente MM, Betsou F, *et al.* Biobanking for better healthcare. Mol Oncol 2008; 2:213–222.

11 •• Bell WC, Sexton KC, Grizzle WE. Organizational issues in providing high-quality human tissues and clinical information for the support of biomedical research. Methods Mol Biol 2010; 576:1–30.
This article describes the major issues that should be addressed in designing and establishing a tissue repository, contains a strong section on quality control and standard operating procedures, and provides valuable insights for all readers.

12 • Blow N. Biobanking: freezer burn. Nature Methods 2009; 6:173–178.
Feature covering a range of topics including sample accrual problems of The Cancer Genome Atlas project, robotic systems at UK Biobank, ambient temperature storage solutions for DNA, and laboratory information management systems for biobanks.

13 • Silberman S. Libraries of Flesh: the sorry state of human tissue storage. Wired Magazine, June 2010. http://www.wired.com/magazine/2010/05/ff_biobanks/all/1.
Problems faced by cryobiologists and biobankers are explained for readers of this popular monthly magazine that reports on how technology affects society.

14 • Hughes S, Barnes RO, Watson PH. Biospecimen use in cancer research over two decades. Biopreserv Biobank 2010; 8:89–97.
This is a survey of biospecimen use described in publications from four major cancer journals between 1988 and 2008. The authors describe an almost four-fold increase in the use of biospecimens over this period, with a growing preference for formalin-fixed, paraffin-embedded tissues.

15 • Moore HM, Compton CC, Lim MD, *et al.* 2009 Biospecimen research network symposium: advancing cancer research through biospecimen science. Cancer Res 2009; 69:6770–6772.
This paper describes the highlights of the symposium. The webcast is archived at http://brnsymposium.com.

16 • Biospecimen Research Database: a joint effort of the Biospecimen Research Network, the RAND Corporation, and the National Cancer Institute Center for Bioinformatics research. https://brd.nci.nih.gov/BRN/brnHome.seam.
This is a curated collection of references to the existing biospecimen research literature.

17 • Yuille M, Illig T, Hveem K, *et al.* Laboratory management of samples in biobanks: European Consensus Expert Group Report. Biopreserv Biobank 2010; 8:65–69.
Discussion of critical issues related to DNA extraction and the management of DNA, plasma, serum and urine samples.

18 • Guerin JS, Murray DW, McGrath MM. Molecular Medicine Ireland Guidelines for standardized biobanking. Biopreservat Biobank 2010; 8:3–63.
This study provides the standard operating procedures for biobanks which cover a range of common biobanking procedures including safety, sample collection and the extraction of molecular analytes.

19 • Barnes MG, Grom AA, Griffin TA, *et al.* Gene expression profiles from peripheral blood mononuclear cells are sensitive to short processing delays. Biopreserv Biobank 2010; 8:153–162.
This report indicates that for samples of peripheral blood, the time between sample acquisition and processing has significant effects on the expression of a variety of genes important to inflammatory, immunological and cancer pathways.

20 • Betsou F, Lehmann S, Ashton G. Standard preanalytical coding for biospecimens: defining the sample PREanalytical Code. Cancer Epidemiol Biomarkers Prev 2010; 19:OF1–OF8.
This study describes a simple code containing up to 13 letters, which describes the pre-analytical variables that correspond to an individual sample. It aimed to facilitate collaborative research in the clinical biobank environment.

21 Betsou F, Barnes R, Burke T, *et al.* Human biospecimen research: experi-
• mental protocol and quality control tools. Cancer Epidemiol Biomarkers Prev 2009; 18:1017–1025.
This paper presents a standard protocol to help reduce variation in experimental design for biospecimen research projects and to facilitate comparison between different studies.

22 Betsou F, Rimm DL, Watson PH, *et al.* What are the biggest challenges and
• opportunities for biorepositories in the next three to five years? Biopreserv Biobank 2010; 8:81–88.
This is the first in a series of articles that invites experts to give their opinions on current issues in biopreservation and biobanking.

23 Vaught J, Baust JG, Heacox AE, *et al.* What are three actionable strategies to
•• improve quality in biomedical research? Biopreserv Biobank 2010; 8:121–125.
This is one of a series of articles that invites experts to give their opinions on current issues in biopreservation and biobanking. This particular article draws attention to the need for more collaboration between cryobiologists and biobankers.

24 Baust JG, Gao D, Baust JM. Cryopreservation: an emerging paradigm change.
•• Organogenesis 2009; 5:90–96.
This is a review of progress in cryopreservation over the 60 years which focuses on recent evidence of genomic and proteomic changes resulting from cryopreservation damage, the link between apoptosis and cryopreservation failure and growing evidence of the detrimental effects of cryoprotection agents like DMSO. It concludes that new strategies for cryopreservation are required.

25 Vaught JB, Caboux E, Hainaut P. International efforts to develop biospecimen
•• best practices. Cancer Epidemiol Biomarkers Prev 2010; 19:912–915.
This paper describes the various best practice guidelines for biobanking, identifies three recurring themes and emphasizes the need for harmonized evidence-based best practices.

26 Wichmann E. Need for guidelines for standardized biobanking. Biopreserv
• Biobank 2010; 8:1.
This is an editorial stating that Molecular Medicine Ireland guidelines have been accepted as the first version of the *BBMRI Laboratory Manual*.

27 Betsou F, Luzergues A, Carter A, *et al.* Towards norms for accreditation of biobanks for human health and medical research: compilation of existing guidelines into an ISO certification/accreditation norm-compatible format. Qual Assurance J 2007; 11:221–294.

28 Vaught J, Kelly A, Hewitt R. A review of international biobanks and networks:
• success factors and key benchmarks. Biopreserv Biobank 2009; 7:143–150.
This is a comparison of the different approaches taken by large biobanks and biobanking networks around the world to the overall management of their operations.

29 Watson PH, Wilson-McManus JE, Barnes RO. Evolutionary concepts in
• biobanking: the BC BioLibrary. J Trans Med 2009; 7:95.
This study describes a new and effective system for linking patient-donors and biobanks called a 'biolibrary' which is an organizational unit that focuses on acquisition, cataloguing and distribution of biospecimens to biobanks.

30 Lee D, Lee Y. The Korea National Research Resource Center. Biopreserv
• Biobank 2009; 7:137–142.
This study describes a Korean network of 33 research resource centres, five core centres and a head office. The resource centres include human, animal, plant, microorganism and nonbiological materials.

31 Watson RWG, Kay EW, Smith D. Integrating biobanks: addressing the
• practical and ethical issues to deliver a valuable tool for cancer research. Nature 2010; 10:646–651.
A review article that highlights issues related to integration of tumour banks.

32 Knoppers BM, Fortier I, Legault D, Burton P. The Public Population Project in Genomics (P3G): a proof of concept? Eur J Hum Genet 2008; 16:664–665.

33 Editorial. Biobanks need pharma. Nature 2009; 461:448.

34 Pálsson G. The rise and fall of a biobank: the case of Iceland. In: Gottweis H, Petersen A (editors). Biobanks. Governance in comparative perspective. 1st ed. London & New York: Routledge; 2008. pp. 41–55.

35 Hansson MG. Ethics and biobanks. Br J Cancer 2009; 100:8–12.
••
This is a concise update on ethical issues in biobanking, including consent, privacy and benefit sharing.

36 ICH Harmonised tripartite Guideline (2007). Definitions for genomic biomarkers, pharmacogenomics, pharmacogenetics, genomic data and sample coding categories, E15. vol. 73. The US Federal Register 2008. pp. 19074–19076. http://www.ich.org/LOB/media/MEDIA3383.pdf.

37 Gottweis H, Lauss G. Biobank governance in the postgenomic age. Personal
• Med 2010; 7:187–195.
This study explores the possibility of lay participation in biobank governance as a means of ensuring public trust and support.

38 Gottweis H. Biobanks in action: new strategies in the governance of life. In: Gottweis H, Petersen A, editors. Biobanks. Governance in comparative perspective. 1st edition. London & New York: Routledge; 2008. pp. 22–38.

39 Hewitt R, Watson PH, Dhir R, *et al.* Timing of consent for the research use of
• surgically removed tissue: is postoperative consenting acceptable? Cancer 2009; 115:4–9.
This study explores practical and ethical issues relating to pre-operative and postoperative consenting and recommends an operational model for postoperative consent.