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Biobanking Trends, Challenges, and Opportunities

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Biobank · Human biomaterials · Biospecimens

Abstract
Objectives: To review the different interests and needs of industry and academic users of human biomaterials. ***Methods:*** A review of the current literature and interviews with involved parties. Questionnaires were e-mailed to assess current attitudes towards biobanking and opinions of trends and implications for the future. The organisations included commercial biobanks, charitable foundations, academic biobanks, and hospital sites. ***Results:*** Biobanks have the potential to have a critical impact across several industrial sectors, and their future success will depend on satisfying the differing needs of each group. There is a growing need for greater collaboration between researchers and biobanks, and if the involvement of industry is not sought by biobanks to create conditions that support the effective use of resources, there is a risk that samples will not be collected or used to the best advantage. ***Conclusions:*** It is evident that industry can play a vital role in the innovation process of biobanking, both in terms of the collecting and processing methods and the nature of the disease and sample types collected. With this feedback, biobanks can be utilised effectively to advance research to the benefits of all to the best advantage.

Introduction

The numbers of organisations involved in the collecting and storing of human biomaterials have significantly increased during the past decade, in line with the increasing use of human biomaterials in research as a replacement to animal models [1]. Limited use of human tissues has in the past been attributed to limited numbers by lack of samples [2], and in particular reliable high-quality, annotated samples [2, 3]. Human materials are now used at an early stage of drug discovery and pre-clinical testing in an attempt to address the high fail rate seen in the past 20 years which has resulted in the so-called 'clinical cliff' [4, 5]. According to Liu et al. [6], '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 safer medical products for patients. This is because the current medical product development path is becoming increasingly challenging, inefficient, and costly. During the last several years, the number of new drugs and biologic applications submitted to FDA has declined significantly.'

Biological marker (biomarker)-based research is being utilised at all stages of the drug discovery process from early-stage drug discovery to clinical trials. By definition a biomarker is a characteristic that can be measured or evaluated as an indicator of a biological process, disease state, or response to a treatment. In the clinic this can be used to monitor or predict responses to treatments [7].

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The growth of translational research and personalised medicine has further increased this demand, and biobanking has been identified as a key area to accelerate growth within these sectors. Biobanks have experienced a huge increase in the amount of samples specifically requested for biomarker and companion diagnostic work. This is driven by the increasing interest in biomarkers to understand and identify the molecular basis of disease. Biomarkers include both genetic biomarkers (e.g. SNPs) and expressed proteins. Oncologists exploit genetic markers clinically to subtype patient populations for therapeutic dosages and to monitor disease progression and severity. The use of biomarkers in such a way is now being applied to other research fields and also at an earlier stage to identify patient groups with a disease risk or stratify patients.

Linked to this is the development of new targets and therapies to treat subsets of patients within disease groups if they have that particular mutation/deficit. As one commercial group interviewed reported, 'Most (clients) want just basic donor information, but for larger studies, especially involving biomarkers, customers want as much information as possible'. To address these issues, drug companies are turning to human samples with detailed donor information to fast-track drug discovery. The use of human tissues is now a 'must have' rather than a 'nice to have' requirement in research projects – it has become the norm for most areas of biomedical research. To overcome the notion of 'buying and selling' human tissue for research use, many biobanks are more comfortable with recovering the costs of collecting, processing, storing, and distributing tissues to biomedical researchers. Funds obtained as cost recovery charges can be used to fund the repository [8].

Methods

Questionnaires were e-mailed to a cross-section of sites in 4 countries that provide human tissue for research purposes. These organisations were selected to represent different types of biobanks including commercial biobanks, charitable foundations, academic biobanks, and hospital sites. The questions were designed to assess current attitudes towards biobanking, opinions of trends within the industry, and implications for the future. A summary of the scope and size of the organisations, together with the questions, can be found in Appendix A.

Biobank Market

The world market for biobanking in human medicine, defined as human tissues, DNA, body fluids, and stem cells for research, therapeutic uses, and biological applications is predicted to generate USD 24.4 billion in 2017 and was worth USD 12.2 billion in 2012 [9, 10]. In response to this demand, biobanks and tissue suppliers have grown exponentially in both numbers and size, and are now established key partners for both academic and commercial groups alike. A recent study of 456 biobanks in the US showed that nearly two thirds of the biobanks were established within the last decade and 17% have been in existence for over 20 years, with 88% of these part of at least one or more larger organisations (67% academic, 23% hospitals, 13% research institutes) [9]. To sustain this level of growth, biobanks have had to understand and satisfy the different interests of their customers in a sustainable method for long-term success. This move away from repository-like organisations and archive libraries is also evident in the level of donor information that is now collected with samples. Biobanks catalogue samples using donor demographics such as age, gender, and ethnicity and may also have information on medical history, genetic traits, environmental factors, and follow-up information. To researchers, this information has become as important as the sample itself and is often a key requirement when sourcing material.

Biobank Growth and Trends

There is now a broad range of suppliers ranging from niche collections who specialise in one disease area to commercial suppliers, and many of these are service-focused organisations. According to a recent report, biobanks have been on the increase since the 1970s with a growth of 42% in 1990–1999 and a further rise in the last decade of 36%, and look likely to continue to expand as researchers continue to favour human tissues and biomaterials for pharmaceutical and diagnostic research [2]. Visiongain, a business information provider based in London (UK) defines the biobanking market as human tissues for research, therapeutic uses, and biological sample banking applications such as DNA and body fluids and stem cells. The report predicts the world market for biobanking in human medicine will generate USD 24.4 billion in 2017 and will expand strongly to 2023 [10]. There is often confusion in regards to what denotes a 'commercial' biobank in comparison with a 'noncommercial' biobank and how operationally these biobanks differ. Commercial biobanks typically procure specimens from primary sources such as hospital clinics. It is difficult to conclude which type of bioresource offers the highest quality of biospecimens; however, commercial vendors tend to be more aware of their inventory and have short-

er lead times related to feasibility studies and to provision of retrospective samples [11]. Virtual biobanks have also increased in number. These biobanks do not store samples but act as a go-between, providing a single point of access to a range of biospecimens. Working with a network of collection sites and biobanks, they virtually source tissues to client specifications without actually collecting or storing samples and deliver them directly to the client. This streamlines the procurement of tissue and benefits all parties, as Labant notes, 'The potential of fulfilling the request and the likelihood of being able to obtain rare samples is greater than going to a single biobank' [3]. Working in this way can be advantageous to both patients and scientists by facilitating wider access to samples.

Consent

One topic of debate is the use of 'broad consent' and whether it can be used to replace more traditional consent approaches. The limitations of defined informed consent becomes apparent when samples are stored for future use as the original consent may no longer be relevant and may limit usage or application if it is not anticipated at the time of sample collection. For some projects, the collection of samples across a cohort can take several years, and new scientific knowledge may come to light during this time. Research knowledge, focus, and goals evolve, often in a way that cannot be predicted. Broad consent typically includes generalities around the nature of future research that might be expected, with the aim of explaining the risks without placing restrictions in place for the future use of the material. Such consent is commonly used in long-term biobanks, recent examples being the UK Biobank, CARTaGENE (Montreal, Que., Canada) and the Norwegian HUNT study. However, there are concerns that broad consent processes lack participants' control and rights over the sample, its uses, and both the research and the results alike. A third model is also emerging – dynamic consent. In dynamic consent, participants are asked for consent continuously, and each new project is a new project. Thus, they will be asked to re-consent both for trivial and essential reasons, and often the former. While dynamic consent provides the research participant with more information than a broad consent process, it is not necessarily respecting the rights and needs of participants in a better way than the broad consent model [12]. Whatever model is used, all information collected is subject to data protection policies and any organisation collecting such information must fulfil their legal obligations to protect that information. Studies undertaken to examine the opinions of donors, and what issues they have relating to consent have shown that concern was more focused on confidentiality issues rather than the consent itself. In particular, where concern was raised, it was most frequently in the area of genomics [13]. The main issues relating to consent balance the depth of information given against the potential need to gather new individual consent for each new application. How broad can consent be without requiring additional consent for specific uses, and alternatively how specific must consent be to ensure the future use of a sample?

Opt-Out

The right to opt out or withdraw consent is a fundamental part of all donor consent forms. The Human Tissue Authority (HTA) states, 'A competent person is entitled to withdraw consent at any time. However, if samples have already been used for a purpose such as research, the withdrawal of consent to any further use does not mean all existing information has to be withdrawn from the research project' [14]. These implications need to be carefully addressed in the consent paperwork with procedures set up and explained, to avoid issues at a later date.

Access to Samples

A major issue that biobanks continue to face is the question of access. Researchers have reported that restricted access to industry partners by some academic biobanks causes difficulties in sourcing samples [11]. Should industry organisations have the same rights to samples as academic researchers? And should access be vetted or controlled in any way? Academic researchers can often obtain samples at little or no cost from academic biobanks and therefore have less need to access samples from commercial biobanks. However, while they have a wider access to samples, this is usually within the constraints of grant-based funding which can impose financial limitations. In contrast, commercial researchers may be less restricted in their budget, but are not as likely to access samples from charitable foundations, not-for-profit organisations, or direct collaborations, as time can be an issue in working in this way. In some cases, access can be through sponsorships where academics obtain the samples, perform the research, and then share the results with the industrial partner. Working with an industrial partner can

add the necessary resources to fund sample collection, but may limit research areas and may restrict publication of the research findings or delay it due to the patenting process [15]. All of the biobanks interviewed, both commercial and not-for-profit, stated they did not make a distinction between any party wishing access to samples, and were of the opinion that everyone should have equal access to samples. It was felt that the priority was to make the best use of samples, and to avoid the potential waste of tissues and biofluids by banking excess surgical/clinical samples. On the whole, samples were collected either on demand for a specific project (with any excess banked) or as surplus tissue that might be of future interest, the latter being the most common. Within the academic biobanks, limitations to sample collection stemmed from lack of resources and resulted in banking the 'easier' samples.

Intellectual Property

Who owns the sample and who owns the data? Ownership and intellectual property is an area of debate that is often raised and can have an impact on where samples are sourced. The complexity lies in the relationship between intellectual property rights and ownership, these rights can relate to the ownership of the samples, inventor or ownership of intellectual property. There was a consensus from all respondents interviewed for this report that biobanks should not claim any intellectual property rights on samples supplied or data derived from them, and that any mention of intellectual property/commercial rights on a transfer agreement presented a significant barrier to sample usage. It was agreed that donors should be told upfront that they would not benefit financially from their donations and that it would be hypocritical/unethical if biobanks then made a claim on their samples for commercial gain. Where research is undertaken, such as development of a cell line, the intellectual property should belong to the innovator and it should be possible to recoup the investment and perpetuate the cycle to the benefit of all parties. As one commercial group reported, 'The reality is that research does not advance in a vacuum. It takes commercial groups to take the financial risk to make them readily available. Companies take samples and isolate difficult cell types, often funded by Federal grants, and commercialize the cells into the research market that might not otherwise be available. We spend the resources to optimize the cell based systems and in return should be able to profit from those efforts'.

Needs of Different Parties: Academics

Within the universities, research-based biobanks are sometimes created by groups of researchers working in similar areas of research. Samples tend to be obtained through direct collaborations between the departments, and hospital samples provided by or to academic institutions are very often nominally priced. The researcher may be directly involved in the collection of samples, which can lead to difficulties in blinding samples and protecting donor information. In most cases, these collections tend to be project specific and related to a certain area of research rather than a disease area and it can be difficult for researchers to obtain the specific number of samples or material from normal donors to validate their results. Normal samples are often more difficult to obtain and are needed to measure selectivity in comparison with diseased samples. The biobanks surveyed reported that most academic requests they received were predominantly for very specific and hard to collect tissues or diseases.

Needs of Different Parties: Pharma

The pharmaceutical industry is in the business of commercialising scientific discoveries and pre-clinical research to develop new drugs. In addition to early-stage drug discovery, samples are also utilised in clinical trials for pharmacogenomic studies to measure the effectiveness of new drug candidates or profile potential side effects. Other commercial users within the biomedical sector such as medical device, diagnostics, biotech, and contract research are similarly focused on bringing products to market. Advances of products at a pre-clinical stage are typically research-based projects done either in-house or through clinical research companies and subcontractors. As a biobank user, these organisations have the resources necessary to fund access to biomaterials, but may not have the time to source or gain access to niche and charity biobanks. In addition, some not-for-profit biobanks require raw data and results be shared at an early stage, which is in conflict with commercial interests. To get around the access issues, some commercial organisations build up their own internal proprietary biobanks created within the frame of specific research projects for internal projects. The biobanks surveyed for this report stated that requests from pharmaceutical companies tend to be broad and are typically for large numbers of samples. Increasingly, requests require very detailed donor information such as survival data, medical history, and pre- and post-surgical data.

Needs of Different Parties: Biotech

Research-based biotechnology companies also utilise human samples and biobanks in their role in the development of new drugs and diagnostics. These companies, often spin-offs from universities, incubate emerging research projects to a more commercial position and subsequently sell or license the resulting products. Due to the origin of these companies, they tend to have close contacts with academic researchers as well as industrial partners, and can act as a third party between the sectors. In this way larger companies can obtain access to academic biobank-based research results and samples. The biobanks surveyed for this report stated that requests from biotech companies tend to require less detailed donor information with requests for de-identified remnant samples with minimal data more common.

Needs of Different Parties: Clinical Research Companies

Clinical research companies undertake research projects on behalf of clients; sometimes these studies are outsourced for reasons of confidentiality, especially for rare disease areas where it might be preferable for a company not to deal directly with the collecting site. As projects are performed on a project-by-project basis, it can be more difficult for clinical research companies to build an in-house resource or biobank due to the variability of the projects. Some companies adopt a strategy where they source samples directly for rare diseases and purchase the more common samples from a biobank. As outputs from these trends, biobanks have experienced an increasing demand for more highly annotated samples. End users have become more 'demanding' in their request in terms of their tissue requirements. For example, a sample of lung tissue is no longer enough; the tissue must come from a specific disease group such as COPD donors, be related to smoking-induced disease, and conform with very specific donor inclusion/exclusion criteria such as the number of packs per day/week and how many years a donor has smoked. Often these collections have to be undertaken as custom collections to these specific requirements.

Predicting Future Sample Needs

All of the parties interviewed agreed that samples are currently collected as a combination of meeting actual or anticipated needs while taking advantage of actual sample availability. As one stated, 'We base what we bank off of either customer demand or as a means of not wanting to waste any donated material'. One not-for-profit service provider whose financial model is based on cost-recovery stated that it was crucial to their existence that they collected what there was in immediate demand to ensure their continued funding. Many of the larger biobanks reported they predict future sample needs by monitoring the market. As one insider put it, 'We attend conferences and monitor the scientific publications to see where we need to make adjustments in our banking'. However, the not-for-profit providers are more likely to bank what is available to them and in going forward it was 'part crystal-ball, part picking up trends in enquiries' with the biggest constraint being limited to what they could collect on site with the available resources. Overall, there was a divide in where the responsibility lay for predicting future sample needs; some felt that the onus was with the biobank to react and others believed that the responsibility was with the end user to drive this change.

Trends in Sample Needs

In terms of sample format, biobanks have seen an increasing need for both fresh-frozen tissue and formalin-fixed paraffin-embedded blocks, and linked to this, formalin-fixed paraffin-embedded blocks with other biofluids such as bloods, urine, and saliva, as well as hair follicles. Fresh-frozen samples are commonly used in biomarker studies or genomic profiling to look for the underlying molecular reasons for disease. Formalin-fixed paraffin-embedded blocks samples are also increasing in demand due to the more standardised processing methods of producing such samples that offer less sample variation and have applications in the histopathological diagnosis of diseases. Biobanks often have large collections of such samples that may date back several decades due to the ease of collection and storage. All of the respondents reported an increase in the demand for fresh samples, and also for more highly annotated samples. No specific disease areas were noted. The developing challenges include the increasing use of neoadjuvant therapy, the decreasing size of tumours, the unavailability of metastatic tissues and of tissues from diseases not treated surgically, requirements to use all of a specific tissue for diagnosis, and the use of fine-needle aspirates for diagnosis. These challenges are driving the increasing development of methods that can utilise paraffin-embedded tissue such as extrac-

tion of mRNA from paraffin sections and its use in real-time reverse transcriptase quantitative PCR. Sample blots, prepared by touching small specimens of tissue on nitrocellulose paper, can also be collected without affecting the diagnostic usefulness of the tissue and can also be analysed by RT-PCR. Also, patients can be requested to donate extra biopsies/fine-needle aspirates during their clinical evaluations to support research [8]. All of these approaches have developed in response to researchers' needs and require collaborative thinking.

Managing Expectations

As sample needs become more specific and client driven, an element of management of expectations may become increasingly necessary. This is especially true in the case of fresh samples. For example, since collecting dorsal root ganglion for research purposes requires the services of a multi-disciplinary surgical team to recover the tissue from a heart-beating donor, a suitable donor must be found whose organs are not suitable for transplant purposes and the collection coordinated within a relatively short window of time. The delivery of the sample may include transport by air which can be constrained by logistics and flight availability. Requests for very low post-mortem intervals or for young donors can be unfeasible due to the time required to get consent from donors and the average age of such donors. Thus, it is important to educate researchers as to those requirements that make their requests difficult or impossible to meet and to search for alternatives [8].

Conclusions

Biobanking has the potential to have a critical impact across several industrial sectors and future success will depend on satisfying the differing need of each group. For continued success, biobanks must have a clear understanding of the needs of researchers, and ensure that the samples and data collected are in line with future research goals. In order to achieve this, researchers both from the industry and academic sectors have to each have their unique needs represented in the biobanking sector, and there is a growing need for greater collaboration. The growth of biobanks will continue to serve biomedical research and it is critical that their ability to serve the research community is not limited by a lack of harmonisation and insufficient representation of researchers' needs.

If the involvement of industry and academic researchers is not sought by biobanks to create conditions that support an effective use of resources, there is a risk that samples will accumulate unused, and opportunities to improve health care will not be created to the best advantage. It is evident that commercial industries can play a vital role in the innovation process of biobanking, both in terms of the collecting and processing methods and giving direction to the nature of samples collected. With this feedback, biobanks will not be in danger of becoming archival libraries and samples will be utilised effectively to advance research to the benefits of all and to best advantage.

Appendix A

Questionnaires

(1) What types of client groups are you seeing and what are the differences in their requests?

(2) Does your biobank make a distinction between access to samples by academics supported by commercial grants or working on behalf of commercial companies or not? Should commercial organisations have the same access rights to samples as non-commercial and academic organisations?

(3) Could you please comment on your current perspectives of the biobanking industry?

(4) How will biobanks have to adapt for future success?

(5) As a biobank, how do you select what samples and/or data to collect? How do you monitor client needs and respond to changes in demand? Have you seen any trends in this area?

(6) Do you have any comments on the intellectual property of data and requirements of some biobanks to supply this? Does it enhance or hinder research? Are there any other issues that should be addressed?

Scope of the Organisations

- UK, France, Germany, and USA
- Charitable foundations
- University-based biobanks
- Commercial biobanks
- Population-based biobanks
- Disease-based biobanks
- Clinical sites with access to diagnostic remnants

Statement of Confidentiality

All parties involved were assured that their comments would remain anonymous unless they otherwise stated they preferred to be named. All parties chose to remain anonymous.

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