The Benefits of Biobanking Human Tissue as a Hub for Future Translational Research

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The pace of translational research has created a need for experimentation on human biological samples. Using such samples can fill the gap between monolayer cell cultures, animal models and testing new treatments in humans, and includes whole organs, tissue, biofluids and their derivatives [1]. Delivery of robust data from these samples relies on providing high quality biospecimens, defined by tissue samples that are linked to detailed records on the tissue collection protocol and allied clinical information, stored in a secure pseudoanonymised format. The parameters that constitutes high quality biospecimens are set by the requirements of advancing experimental techniques and key regulatory stipulations. The 2007 European Union Tissue and Cells Directive and the UK 2004 Human Tissue Act (HTAct) set the regulatory framework and have resulted in a climate where biospecimens are increasingly processed and stored in large centralised facilities (in place of small local stores) [2]. These facilities take advantage of economies of scale and are better able to meet regulatory requirements and quality needs of researchers. However, the rise of such facilities has presented a number of challenges that can be categorised into three areas: (1) delivery of useable samples to promote translational research; (2) sustainable business models; (3) obtaining informed consent and ethics.

Biobank model

A common biobank model involves collecting a biospecimen from tissue removed during surgery that is surplus to diagnostic requirements, or taken alongside conventional medical testing (e.g. blood and urine). Biospecimens can be used fresh or stored in biobanks, often as fixed blocks or cryopreserved where the specific collection conditions, allied clinical and life style information is linked to each sample. The allied information allows researchers to assess the context of their findings, whilst detailed collection information ensures their data is robust. With well administered and integrated systems, this model can deliver highly quality biospecimens.

Researchers, clinicians and healthcare professionals involved with breast cancer care have recognised the need for high quality biospecimens through biobanking. Until relatively recently, research into BRCA 1 and 2 had primarily focused on investigating the cellular function of the multi-domain proteins, leading to some important new treatments. However, only a small proportion of breast cancers develop due to a loss of BRCA function, mainly resulting from somatic mutations or changes in expression of other genes [3]. Testing on biospecimens could provide a way to relate cellular signalling pathways and changes in beast architecture, spatial, temporal and differential control of gene expression. Data from such experiments can then be linked to other studies, such as DNA analysis from cancer prevention trials and clinical trials for radiotherapy and chemotherapy that link DNA variants to treatment responses [1].

Sharing of the datasets

To facilitate sharing of datasets and to truly realise the translational potential of biobanks, it could be argued that data from researchers should be returned to the biobank and linked to the original biospecimen. Biobanks are perfectly placed to become custodians of both biospecimens and associated datasets, resulting in a significant increase in research value. For example, published trial results from UK, Europe and the US can be complimentary, although there are limitations to accessing robust data from different sources, pointing to a need for greater international exchange of information. Commonly, data on biospecimens are either part of intellectual property or are selectively published in academic journals (i.e. predominantly positive data) [4]. Efforts to share data are already underway, notably the Breast Cancer Tissue Bank established in 2010, which has a two year time limit on returning experimental data on tissue obtained from the biobank [5]. Furthermore, if the resulting data sets are stored in the biobank for later data mining, the research value for each donation can be significantly increased. Encouraging such a system will need buy in from private and public sector researchers, a proposition that requires further exploration, although this is a model under consideration as part of the University College London Tissue Access for Patient Benefit Project.

Sustainability

Returning results and offering high quality biospecimens forms is part of adding value to biobanks that should enable them to become self-sustaining entities, especially in a climate of financial restrictions in healthcare and research. Many standalone biobanks need additional funding to support their activities. Furthermore, there have been cases where biobanks prospectively collect tissue over many years only to discard biospecimens due to the lack of adequate management systems. At the same time many commercial researchers are desperately seeking high quality biospecimens to perform pre-clinical and clinical trial experiments to bring new treatments to market [6]. The future for biobanks may lay in diversification of research activities around centralised infrastructure that benefit from automation and integration to increase efficiency and quality of samples. For example, the efficiency of a single tissue collection can be optimised by using existing facilities associated with healthcare institutions (e.g. histology, biochemistry and clinical trial infrastructure), as well as allowing a number of researchers to perform a whole range of studies on a single set of biospecimens.

Furthermore, the transition from centrally funded biobanks to self-sustainability needs the adoption of business models that can release the research value

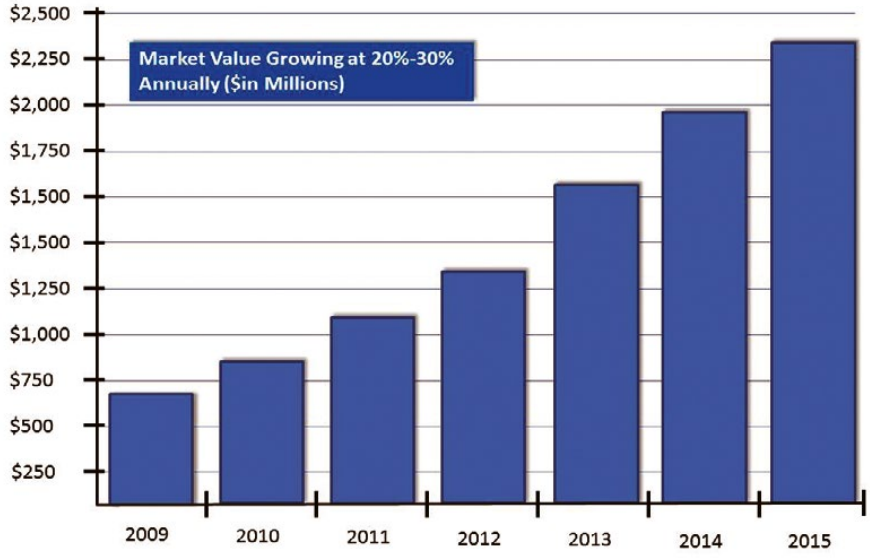

Figure 1: The increase in value of the USA Biobanking Market [7].

within biospecimens and attract private sector researchers as well as academic projects. One option could be to oblige data sharing arrangements, albeit non-commercially sensitive data sharing, where the added research value for biospecimens could lead to more sustainable biobanks. Another important consideration is calculating the true cost of biobanking, for example devising the Total Life Cycle Cost of Ownership (TLCO). Using TLCO the costs of owning, operating and maintaining a tissue provision service is compared against potential income generation by adding research value to biospecimens through diversification of activities and support services. However, the current lack of data on costs and associated outcomes, makes calculating the TLCO difficult. This is mainly due to most biobanks being born out of research department with sustainability as a standalone entity not being the main focus, with many hidden costs paid for by the supporting institution. One encouraging trend that illustrates the potential for biobanks to become self-sustainable is the increasing biobanking market for the use of human tissue in drug discovery and preclinical trials (Figure 1). Many challenges remain, however, owing to the incredibly fragmented nature of the industry exemplified by no one institution having more than 3% share of the biobanking market in the US. There is also a lack of standardised collection and storage protocols quality or data integrity [5,7].

Ethical issues and consent

With expanding use of biospecimens and associated data there is clearly a need for researchers and biobanks to ensure patients are actively involved with these developments. The 2004 Human Tissue Act (HTAct), National Ethics Review Service and the Nuffield Council of Bioethics approve of researchers obtaining generic consent from patients to use their tissue for future ethically approved research. The process involves prospectively collecting biospecimens to be held within a licensed biobank, for researchers to then apply to the biobank for ethical approval to use the samples [2,8]. There are critics of generic consent, describing it as not being truly "informed" consent (a stipulation of the HTAct) as the future research cannot be defined, therefore suggesting alternatives such as opt-in and tiered consent [9].

Opt-in consent involves asking the patient whether they would allow their tissue to be used for a specific research project. Each additional project would need the researcher to approach the patient for renewed consent. The main disadvantage is the potential for valuable biospecimens to be discarded after a research project ends, thereby increasing the cost to output ratio of the research project.

Alternatively, tiered consent is a more restricted form of generic consent that allows the donor to agree to the use of their samples in unknown future projects, but gives the option of specifying particular categories of research that they wish to exclude, e.g. embryonic research or commercial research. Tiered consent can be complex to administer without sophisticated IT systems to track consent. Most licensed biobanks offer a mixture of generic and tiered consent, with many opting to refuse patients who place stipulations over and above what an ethical review board would approve.

Studies surveying UK Adults showed 55% in favour of opt-in consent, although with greater discussion less restrictive models of consent became more acceptable[10]. A similar study across Europe showed between 69-95% support for generic consent (depending on country)[11]. As a whole there is a preference amongst the UK public for on-going choice and control over donated biospecimens. One suggested method of allowing greater involvement is to create a Wiki style governance structure, where the biobank governance policies would be made available online, for any registered participants to modify and discuss on an online forum. Once a consensus has been reached a biobank committee would act as final arbiters to decide whether the policies are scientifically, ethically or legally valid[12].

The biobanking sector is at the beginnings of an exciting journey towards forming the cement between platforms used in translational research. As they develop and expand, involving all the stakeholders for research using human tissue is crucial in ensuring sustainability and increased research value. The most important stakeholder is the patient or volunteer who must maintain trust in the system, a challenge that can only be tackled through robust informed consent pathways and public awareness campaigns and total transparency. ■

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