Insight Series

The Issue with Tissue

Recommendations for improving the use of human tissue samples

use MY data

INCISIVE HEALTH

CATAPULT Medicines Discovery

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Introduction

The availability, and utilisation, of human tissue samples is essential for making progress in medical research.[1] Samples are used throughout the process of developing treatments, from improving researchers' understanding of how diseases develop, to establishing how drugs will affect disease and impact on other areas of the body.[1]

When patients donate their tissue samples, they are making an important contribution to improving the treatment and care of future generations. However, it has been estimated that only 15% of samples donated for research are ever used.[1]

Too many samples are stored but not used. Researchers and innovators report facing bureaucratic barriers to accessing tissue samples. These challenges range from finding appropriate samples to setting up the legal agreements for use.

This hinders both the speed and quality of scientific research, damaging the UK's position as a centre of research and innovation excellence. It also frustrates the wishes of the patients who donate their samples, wasting their time and generosity.

The issue with tissue must be addressed as a matter of urgency: patients are determined to seek change. They are concerned that this situation frustrates their wishes, and undermines the important case for tissue sample donation: if samples are not used, why bother donating?

After initial discussions at a use MY data workshop in 2018, use MY data, Medicines Discovery Catapult (MDC) and Incisive Health facilitated a workshop in September 2019 to seek solutions. The attendees are listed in the Appendix.

The discussion was guided by twin objectives:

- Every sample in the UK should be discoverable
- The success of biobanks should in part be assessed by published usage rates

[1] Discussion at use MY data's 'Your data, your control' workshop, May 2018

"There is a responsibility for those holding information to do something with it, because nobody wants to give their data, or their samples, and then nothing happen with it"

Patient Advocate,
use MY data

"There is a lot of talk about consent for use, but I don't want to give consent. When I donate, I want to give an instruction. Use my tissue to benefit others!"

Patient Advocate,
use MY data

During the workshop, 10 actions were identified to address the issue with tissue:

1. A strategic needs assessment should be undertaken to establish the types of sample that should be prioritised. Samples currently in storage should be audited and assessed for utility
2. Hypothesis-driven collection should be encouraged wherever possible, whilst recognising the value of retrospective sample sets and collection without a pre-determined use for rare conditions
3. The opportunities created by digital pathology should be seized to ensure greater involvement of expert pathologists in guiding sample collection. In order to support this, a programme of engagement between tissue banks and pathologists should be undertaken
4. Tissue bank registration with the national directory should be made mandatory, and the option to "opt-out" when registering with the Health Research Authority (HRA) removed. As a first step, registering with the national directory should be made a condition of funding and ethics approval and a list of non-registered biobanks should be developed and shared with HRA and research funders
5. Common ways of cataloguing and publicising samples should be encouraged, to reduce variation in process across tissue banks. All banks should publish the number and type of the samples they hold, as well as the disease and/or patient characteristics of the samples, details of permission and the process for gaining access
6. Tissue banks should be required to publish how many samples they collect and how many they release (a "tissue turnover rate"). Acknowledging this rate could be used as an over simplistic measure, it should be recognised that different rates may be appropriate for different forms of tissue banks. Banks should also publish a commentary explaining their rate and setting out plans to encourage greater release where appropriate. Response rates to queries should also be published
7. Work should be undertaken, and templates developed, to better standardise and improve the efficiency of application processes, including permission forms, access policies, Material Transfer Agreements (MTAs) and timelines for release. Where possible, this activity should build on work previously done
8. Funders should recognise that transparency will have costs, although in time it will lead to greater efficiency. The resource implications of transparency should be reflected in grants and ongoing support for tissue banks. Where transparency is administratively arduous for smaller banks or individual collections, collaboration with the Tissue Directory and Coordination Centre (TDCC), larger banks or long-term storage options should be encouraged
9. Patient samples should be acknowledged in research. The use MY data "patient data citation" could be adapted to tissue samples. use MY data is consulting their members to produce a tissue citation. Similarly, tissue banks that have released samples should be recognised in research papers by authors, for example, they could be named as a collaborator
10. The results of research that has used tissue should be more widely publicised, to recognise the role of both patients and tissue banks. Lay summaries of research findings should also be made available on a searchable database so that patients may understand how samples similar to theirs are advancing research. A "Tissue Donor Week" could be established, where different parts of the system publicise their work, including through the development of a full range of case studies, and how this serves to progress research

These recommendations have been designed to be achievable in the current context. While some have implications in terms of funding and time which are important to recognise, they will lead to greater efficiency within the system.

These changes could be achieved through voluntary action. However, should this not be forthcoming, there is a case for amending human tissue legislation to ensure high standards of transparency and to make clear that there is a duty to use samples well, and hold them securely.

Improving access to tissue samples

Steps can be taken to improve access to tissue samples at every stage of the donation and release pathway, as set out below:

Patient donates their tissue in the course of diagnosis or treatment

Ensuring samples are fit for purposes for modern science

Enabling researchers to identify relevant samples

Releasing samples to the researchers who need them

Some tissue samples are never requested

Recognising and feeding back the role of tissue samples in research

Who's who in the tissue donation and release pathway

- **Health Research Authority (HRA):** protects and promotes the interests of patients and the public in health and social care research. The HRA organises the ethical review of research including tissue collection or biobanking, and has priorities around increasing research transparency and promoting the sharing of data from research
- **Human Tissue Authority (HTA):** the regulator for tissue and organs, responsible for all aspects of human tissue and organ use, including anatomy, public display, human application, post mortem, organ donation and transplantation, as well as research. The HTA covers organisations that remove, store and use human tissue for research. It licenses premises that take and store human samples, but does not license the use of samples or the ethical approval for research
- **Patients:** consent for the use of their samples in research. They are often represented on individual biobank management and access groups, but they have no formal way of changing the overall system
- **Biobanks:** in most cases, Biobanks can only use samples for specific reasons stated in the consent form. If the consent is broad and the bank has an HRA status of "research tissue bank", biobanks are able to approve which researchers can use the samples
- **Research funders:** fund research, often including biobanking. They can include terms in the funding such as sample accessibility, though the policing of these terms is unclear

Key stages on the journey to using a tissue sample

Donation

Tissue donation is a success story in the UK. About 1 million patients have consented to their samples being used specifically in research studies. There are a further 3 to 5 million samples held in tissue banks in the UK, where patients have permitted their sample to be used in future studies.[1]

Although there is more that can be done to improve donation rates, with the associated collection of donations having resource and capacity implications for NHS hospitals, this is not where the primary problem lies.

Ensuring samples are fit for purpose for modern science

Medical research is a fast-moving field, and it can be difficult for tissue banks to make sure the type and form of samples collected keep pace with the requirements of modern science. It is also important that the quality and data completeness of samples is high. Tissue should be accompanied by relevant information about the nature of the patient and their illness.

Usefulness, rather than quantity, should be the focus. To ensure the use of tissue samples being collected and held in the UK, the following actions should be considered:

1. A strategic needs assessment should be undertaken to establish the types of sample that should be prioritised. Samples currently in storage should be audited and assessed for utility
2. Hypothesis-driven collection should be encouraged wherever possible, whilst recognising the value of retrospective sample sets and collection without a pre-determined use for rare conditions
3. The opportunities created by digital pathology should be seized to ensure greater involvement of expert pathologists in guiding sample collection. In order to support this, a programme of engagement between tissue banks and pathologists should be undertaken

Enabling researchers to identify relevant samples

Many tissue banks have developed as a result of the initiative of individual or groups of researchers. While this is commendable, it has resulted in a fragmented system of storage and access. It can be difficult for researchers and innovators to identify which samples may be relevant to their work. Research by the National Cancer Research Institute CM-Path has estimated that around 50% of samples cannot be found on a web directory.[2]

It is important to recognise there are costs associated with running tissue banks, including storage, refrigeration and monitoring. Unless samples are readily available for use, these are wasted resources.

In response to these issues, a national directory has been set up, managed by the UK Clinical Research Collaboration Tissue Directory and Coordination Centre (UKCRC TDCC). However, a significant subset of tissue banks have not submitted the data to make their samples accessible, perhaps due to a lack of resource. To counter this, there needs to be a clearer understanding of the expectations on a tissue bank, as opposed to samples collected for use in only one research study.

Even when a sample can be found, it can be challenging for a researcher to identify the right person to contact, and what the criteria for access would be. To address the challenges in cataloguing samples and informing the system about their availability, the following actions should be considered:

4. Tissue bank registration with the national directory should be made mandatory, and the option to "opt-out" when registering with the HRA removed. As a first step, registering with the national directory should be made a condition of funding and ethics approval, and a list of non-registered biobanks should be developed and shared with HRA and research funders

[1] Discussion at use MY data's 'Your data, your control' workshop, May 2018

[2] NCRI CM-Path, Improving the discoverability of cancer biobanks,The Bulletin of the Royal College of Pathologists, Number 186, April 2019

Releasing samples to the researchers who need them

There is also a range of barriers hindering the release of tissue samples from tissue banks. There is a potential conflict of interest where banks are led by researchers with a specific interest, as they have to balance releasing samples to researchers in their field, or keeping them in case they are of future use for their own academic work.

Feedback from researchers highlights that the process of release can be costly, bureaucratic, and often lacking transparency. When trying to access samples, researchers and innovators are sometimes faced with confusing criteria for release or unclear timelines. Brokered sample access can be considered to support tissue banks with the contractual and logistical arrangements of making samples available to researchers in a timely fashion, but not all banks take up these services.

Transparency – and the concept of 'publish and explain' – must be the guiding principle in the release of tissue samples. This could build on the work done by the TDCC to encourage self-reporting by biobanks.

The following steps should be considered:

5. Common ways of cataloguing and publicising samples should be encouraged, to reduce variation in process across tissue banks. All banks should publish the number and type of the samples they hold, as well as the disease and/or patient characteristics of the samples, details of permission and the process for gaining access

6. Tissue banks should be required to publish how many samples they collect and how many they release (a "tissue turnover rate"). Acknowledging the risk that this rate could be used as an over simplistic measure, it should be recognised that different rates may be appropriate for different forms of tissue banks. Banks should publish a commentary explaining their rate and setting out plans to encourage greater release where appropriate. Response rates to queries should also be published

7. Work should be undertaken, and templates developed, to better standardise and improve the efficiency of application processes, including permission forms, access policies, Material Transfer Agreements (MTAs) and timelines for release. Where possible, this activity should build on work previously done

8. Funders should recognise that transparency will have costs, although in time it will lead to greater efficiency. The resource implications of transparency should be reflected in grants and ongoing support for tissue banks. Where transparency is administratively arduous for smaller banks or individual collections, collaboration with the TDCC, larger banks or long-term storage options should be encouraged

Common ways of cataloguing and publicising samples should be encouraged, **to reduce variation in process across tissue banks**

Recognising and feeding back the role of tissue samples in research

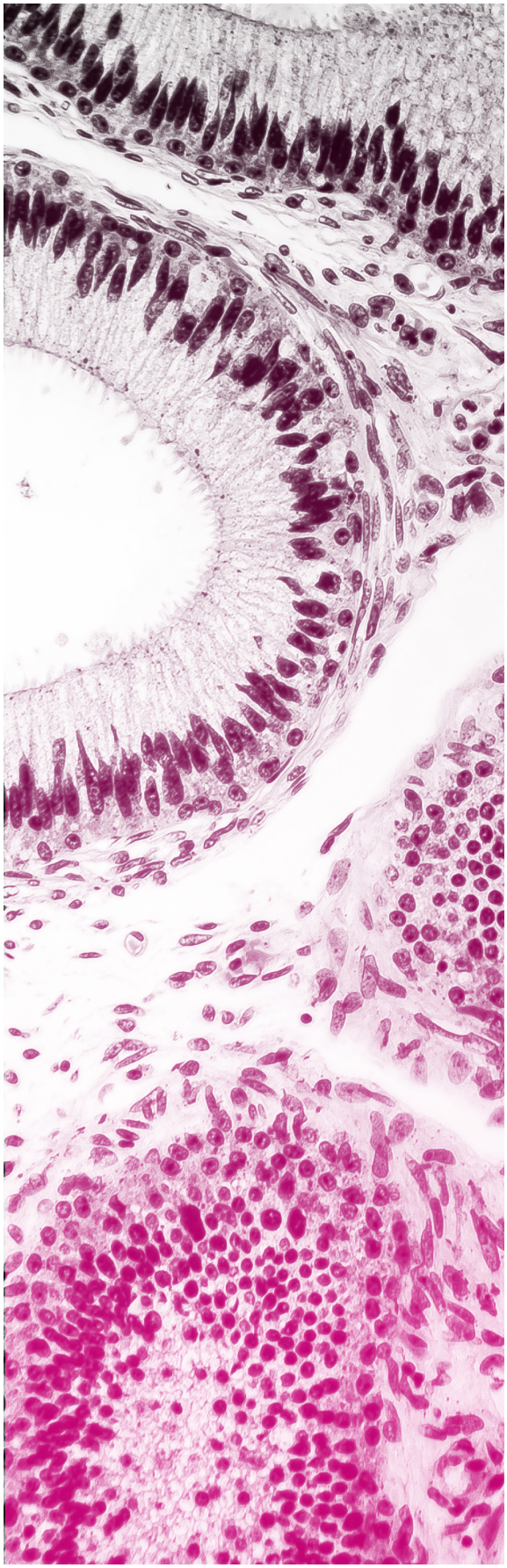
Research involving human tissue is only possible because people donate samples. It is important that feedback is provided on the impact of the donation.

By publishers acknowledging the contributions of tissue banks to research, the patients who have donated to such banks can gain a greater understanding of how their donations have been used to benefit others. By acknowledging where a sample has come from, researchers can foster a more collaborative culture, recognising the important role both of donors and tissue banks.

The following actions should be considered:

9. Patient samples should be acknowledged in research. The use MY data "patient data citation" could be adapted to tissue samples. use MY data is consulting their members to produce a tissue citation. Similarly, tissue banks that have released samples should be recognised by authors in research papers, for example, they could be named as a collaborator

10. The results of research that has used tissue should be more widely publicised, to recognise the role of both patients and tissue banks. Lay summaries of research findings should also be made available on a searchable database so that patients may understand how samples similar to theirs are advancing research. A "Tissue Donor Week" could be established, where different parts of the system publicise their work, via a full range of case studies, demonstrating how this serves to progress research



Next steps

It is important that engagement takes place with all parts of the research community. There is a need to explore these potential solutions in more detail, and to hear the thoughts of stakeholders on how we can best resolve the issue with tissue.

Appendix – About the Issue with Tissue workshop

The workshop was supported by MDC and by an unrestricted grant from Roche Products Limited. Roche did not participate in the workshop and had no input to the content. Incisive Health provided support through reduced fees.

The following attendees participated in the workshop:

- Erinna Bowman, UK Clinical Research Collaboration Tissue Directory and Coordination Centre
- Chris Carrigan, use MY data
- Dr Claire Eckert, University of Leeds
- Dr Richard Evans, Medical Research Council
- Eleanor Garratt-Smith, Breast Cancer Now
- Sheila Graham, Newcastle upon Tyne Hospitals NHS Foundation Trust
- Professor Andy Hall, National Cancer Research Institute CM-Path
- Joanne Hartley, Medicines Discovery Catapult
- Helen Hind, Medicines Discovery Catapult
- Dr Sarah Markham, King's College London, use MY data
- Dr Morag McFarlane, Tissue Solutions
- James Peach, Independent
- Henry Scowcroft, Cancer Research UK
- Dr Hayden Selvadurai, Ervaxx
- Richard Stephens, use MY data
- Alison Stone, use MY data
- Lesley Turner, use MY data
- Sophia Turner, use MY data
- Dr Ian Walker, Cancer Research UK

The workshop was facilitated by Mike Birtwistle, Incisive Health. The workshop was observed by:

- Elizabeth Beck, Incisive Health
- Laura Tantum, Incisive Health

Some participants attended in an independent capacity and some participated on behalf of their organisation, but the views expressed in this report do not necessarily represent those of any particular organisation.

References

[1] Discussion at use MY data's 'Your data, your control' workshop, May 2018

[2] NCRI CM-Path, Improving the discoverability of cancer biobanks, The Bulletin of the Royal College of Pathologists, Number 186, April 2019

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