9. Biosample Provenance: What Researchers Need To Know

Robert Hewitt

Published April 15th, 2019

Every biosample used for medical research has a different journey. The journey starts when the sample is donated by a person. The journey ends when the sample is analysed in a research laboratory. In between, there are a wide variety of possible routes, events and timelines, all of which may have the potential to affect the sample quality. Details of the sample journey need to be recorded for a variety of reasons, not only for scientific reasons (relating to quality control for example), but also for legal and ethical reasons, as explained below.

The word 'Provenance' is important here. According to the Merriam-Webster dictionary, it means the origin or source of something. In the world of antiques, the word provenance means the history of ownership of a valued object or work of art. According to the World Wide Web Consortium, provenance includes:

'... information about entities, activities, and people involved in producing a piece of data or thing, which can be used to form assessments about its quality, reliability or trustworthiness'.

From the research scientist's perspective, the provenance of biosamples includes four types of information about the samples:

(1) Geographic origin

(2) Previous custodian(s)

(3) Sample processing history

(4) Donor information

Each of these will now be discussed in turn:

1. Geographic Origin

Knowing the country of origin of a biosample is important because this may provide information about environmental, socio-economic and genetic factors that will help make sense of research findings. It is also important to know if samples come from specific countries that have legal restrictions on export (for example, China, India and Russia), as in these cases it will be necessary to double-check that the samples have been exported in a manner that respects the national regulations (Cooreman et al, 2017).

2. Previous Custodian(s)

The researcher needs to have information about all previous custodians of the sample, to be confident that the sample has been (a) obtained ethically and (b) processed reliably.

For samples to have been obtained ethically, sample donors must have provided informed consent and the sample collection operations must have had ethical oversight and approval. This is in line with the following regulations and guidelines:

- US revised Common Rule effective July 19, 2018
- European Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin.
- UK Human Tissues Act (2004).

Evidence of compliance should be provided by the source biobank.

For samples to have been processed reliably, they must have been collected according to well established standard operating procedures in an organisation with quality assurance measures in place. If the source biobank has obtained appropriate certification, accreditation, or licensing, this gives confidence about sample quality and reliability. For example:

- US CAP Accreditation for Biorepositories
- International CTRNet Certification of Biobanks
- International ISO 9001:2015 which sets out the criteria for a quality management system
- International ISO 20387:2018 which specifies general requirements for the competence, impartiality and consistent operation of biobanks including quality control requirements to ensure biological material and data collections of appropriate quality.
- Licensing by the Human Tissue Authority in the UK.

In order to recontact the biobank for additional samples or sample/clinical information, you will need to know the identity of the source biobank. This is also necessary in order to give proper credit to the source biobank in publications. It is 'best practice' for biobanks to require you to sign a material transfer agreement (MTA) in order to receive samples. This document will contain a lot of important information relating to restrictions on use, requirements for maintaining privacy and confidentiality, requirements for appropriate biosafety knowledge for handling, as well as other factors.

If samples have been obtained from a commercial biobank, then this intermediary organisation must agree to be sufficiently transparent to provide information about the source biobank as well as information about any additional intermediary organisations that may have been involved in sample procurement.

3. Sample Processing History

Even in the simplest cases, there is huge potential for variation in sample processing. Take for example the resection of diseased tissue by a surgeon. Not only is there the warm ischaemia time to be recorded (from the time that blood vessels are clamped to the time of surgical resection), but also there is the cold ischaemia time (the time the sample is transported on wet ice before freezing). Both of these times will vary from case to case and may affect sample quality. Then there is the transfer of the sample on dry ice to the requester which may involve shipping delays, again potentially affecting sample quality. If samples require additional processing in the biobank, as in the case of blood samples requiring fractionation, then this has the potential to introduce additional variation between samples, especially if samples come from different biobanks using different protocols. To take these preanalytical factors into account, a Standard PREanalytical Code (SPREC) was developed and is used by some professional biobanks (Betsou et al, 2010).

Specific information about sample processing history should be provided by the biobank and as mentioned before, if appropriate certification or accreditation has been obtained, this will give confidence about sample quality and reliability.

4. Donor Information

It will be necessary to have information about the sample donor, which may be demographic information and in the case of patients, their clinical history. Before this information is provided to you, the identity of the donor must be protected by either

anonymizing or pseudo-anonymizing this information in line with with the following regulations:

- US Health Insurance Portability and Accountability Act (HIPAA).
- European General Data Protection Regulation (GDPR).
- UK Data Protection Act of 2018.

If you require additional information about the patient in the future (eg. for disease-free remission period or survival data) then you will need to know the identity of the source biobank. If you obtained samples through a commercial intermediary, then you will need their support in contacting the source biobank for this information.

Conclusion

Information about biosample provenance is necessary for researchers to draw conclusions from their analysis. It is obviously essential to have information about the donor of the sample, so that research findings can be interpreted correctly. In addition, information about biosample provenance allows the researcher to be confident about the quality of the samples, the reliability of the samples for use in particular studies, and the trustworthiness of custodians who collected, processed, stored and/or procured the samples.

Researchers who do not have adequate biosample provenance information, are at risk of producing research that is irreproducible.

Freedman *et al* (2015) analysed the categories of errors that contribute to irreproducibility of US preclinical research and concluded that errors due to 'biological reagents and reference materials' form the most important category. Furthermore, they assert that immediate steps to rectify this category of errors will provide significant return on investment and substantial improvements in reproducibility. They go on to say that:

' … the challenge of increasing reproducibility and addressing the costs associated with the lack of reproducibility in life science research is simply too important and costly to ignore. Lifesaving therapies are being delayed, research budgets face increasing pressure, and drug development and treatment costs are rising. Improving reproducibility remains a critical cornerstone to solving each of these challenges.' Freedman et al (2015). The Economics of Reproducibility in Preclinical Research.

By demanding adequate provenance information on biosamples, researchers can help combat this major problem of irreproducibility in preclinical research.

****

Disclaimer: the author of this article works independently and any views expressed are his own.

All 10 Articles In The 'Biobanks & Industry' Series

1. Why Biobanks Should Provide Biosamples to Industry
2. Ensuring Public Support for Biobank Cooperation With Industry
3. The Main Actors Providing Biosamples to Industry
4. Biosample Needs of Different Industry Players
5. The Dual Role of Academic Biobanks
6. What is Commodification?
7. Acceptable Transactions in Biobanking
8. Why Biobank Access Policies Should Be Publicly Available
9. Biosample Provenance: What Researchers Need To Know
10. Biosample Supply Problems Affecting Industry Research And Tomorrow's Patients

To see these articles click here: https:/www.biosample.net/articles/