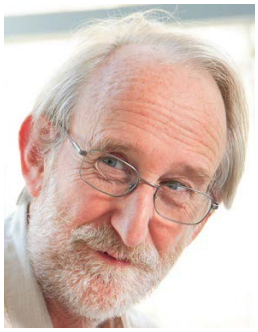
Improving the discoverability of cancer biobanks

To serve researchers effectively, research tissue banks need to be visible and provide information on samples held and how to access them. This article describes an online review of how many cancer biobanks fulfil these criteria and suggests improvements.



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Background

Translational research aimed at improving outcomes in rare cancers is hampered by the challenge of assembling cohorts of tumour samples large enough to produce statistically robust results. Similar problems are becoming commonplace in the study of subgroups within common tumours with differing response to treatment.

Charities such as Breast Cancer Now, Bloodwise and the Pancreatic Cancer Research Fund have addressed this challenge by supporting the formation of national research tissue banks (RTBs), which facilitate access to samples by academic and commercial research groups, both in the UK and abroad. In addition, work undertaken by the Health Research Authority (HRA) and Human Tissue Authority has created a regulatory environment that supports these initiatives through the licencing and inspection of premises for the collection and storage of human tissues for research and through the RTB ethical approval process. This allows biobanks to supply tissues for research programmes without the need for additional Research Ethics Committee (REC) approval.

In 2011, the report *UK Funders' Vision for Human Tissue Resources* from the UK Clinical Research Collaboration (UKCRC) highlighted the need to 'improve the UK's effectiveness in collecting and using tissue'.[1] One of the key recommendations was the need to make sample collections 'more easily discoverable and accessible for use in high quality, ethical research' through the establishment of a publicly accessible directory.

As a result, the UKCRC Tissue Directory and Coordination Centre was established in 2015 to provide an open-access site for registering sample collections that can be used by researchers to identify potential sources for the samples they need in their research.[2] Registration on the site is now a condition of ethical approval for an RTB. However, the 2018 State of the Discovery Nation survey indicated that 80% of UK small and medium enterprises found accessing UK samples unexpectedly difficult.[3] The authors, on behalf of the National Cancer Research Institute's Cellular and Molecular Pathology Initiative and the Medicines Discovery Catapult, therefore carried out a piece of work to assess the quality of information provided by RTBs about the nature of the samples they provide and the requirements for access.

Assessing the quality of information provided by the RTBs

Interrogation of the HRA database

We identified RTBs with NHS Research Ethics approval using the database produced and hosted by the HRA, which includes summaries of all applications made since 2008.[4] Of the 31,176 applications listed on 19 August 2018, 239 were flagged as RTBs. We used the title of the application and text under the headings 'data collection arrangements' and 'research programme' to identify 81 banks as potentially including cancer samples. Of these, 23 had no text to describe the purpose of the collection and a further six had only brief details (fewer than 50 words).

Interrogation of the UKCRC Tissue Directory

Interrogation of the UKCRC Tissue Directory revealed that 39 of the 81 possible cancer biobanks were included on the database. Five had only limited information regarding the purpose of the bank. Twelve had no website link and in two cases the link was not working. Of the 25 banks that had included a link, four were to sites not specifically dedicated to RTBs.

Identification of biobank websites using a search engine

We used Google to try to locate websites for RTBs listed on the HRA database that were either not listed on the UKCRC Tissue Directory or had tissue directory entries without working links. For 30 of the 81 RTBs listed, no further information could be found using a simple search on the title of the collection used in the research ethics application. For the 51 banks where information was available on the web, we were able to deduce that 45 of the HRA-approved RTBs were likely to include cancer samples. Results are summarised in Figure 1.

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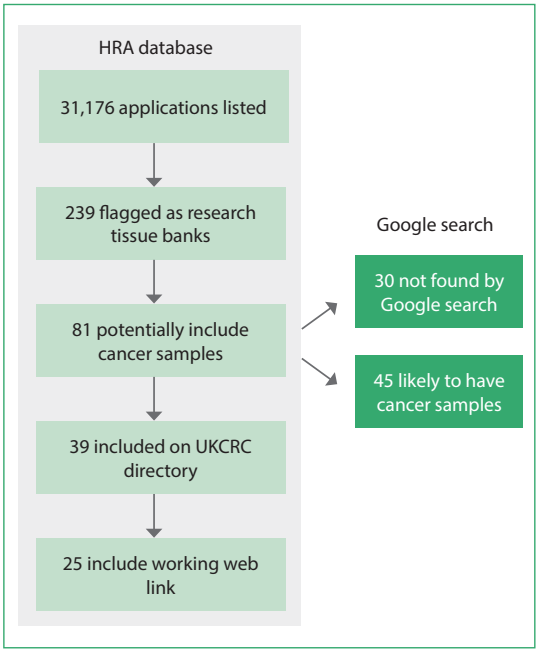

Figure 1: Summary of results obtained from the HRA database of applications for ethical approval of an RTA.

Assessment of the information provided on biobank websites

The quality of information provided to researchers outside the host institution was assessed on the 45 websites identified above under the following.

1. The type of samples included in the biobank:
   - cancer type
   - sample type.
2. The level of access:
   - local only
   - only if working with local teams
   - open (including after assessment for scientific validity).
3. The process for applications from commercial organisations.
4. The method of assessment of applications:
   - independent panel
   - curator/management group only.
5. The ethical approvals required:
   - covered by the RTB (if within the scope of their approval)
   - separate ethical approval required.
6. Price or estimates of costs of access.
7. Email or telephone information for access.

Using these criteria, an overall assessment was made of the quality of information provided. Results are shown in Table 1.

In four cases, it was clear that access was for local researchers only. In 24 cases, it was unclear whether commercial organisations could apply. In 15 cases, the research tissue bank indicated that they were able to include applications to use samples within their ethical approval from the NHS REC. In two cases, the need for separate approval was specified. In the remaining 28 cases, the requirement for ethical approval was unclear.

Information was given on 15 websites about the approval of applications, but the approval process was not specified. Of the remaining sites where access was granted to external applicants, assessment was performed by an independent panel at 25 sites, while two others indicated that this was at the discretion of the biobank management. Ten websites indicated that a charge would be made to access samples, to recover the costs incurred in operating the biobank; no indication of pricing was given.

How can things improve?

The establishment of the UKCRC Tissue Directory was a major step forwards in making sample collections more discoverable – a key action point in the 2011 *UK Funders' Vision for Human Tissue Resources*. Registration on the directory is now a mandatory requirement for NHS Research Ethics approval and the number of registered collections has reached a level to make the directory a valuable resource for researchers. However, its value is depends highly on registration rates and the level of detail provided on the site or on associated websites.

Although some excellent websites have been developed by biobanks (see, for example: www.ethicaltissue.org, http://orb.ndcls.ox.ac.uk, www.breastcancertissuebank.org), our survey has identified major shortcomings in the quality of web-based information provided to researchers by RTBs in the cancer sector. We were only able to identify 16 banks with sites that didn't have significant omissions in the information provided. Of these, three are not currently listed on the UKCRC Tissue Directory and seven had no text on the HRA database describing the collection. The ability to

Table 1: Assessment of biobank websites.

Assessment	Number of sites
5* All relevant information easily accessible	10
4* Well designed site with only minor omissions	6
3* Most information included but not all easily discovered	6
2* Significant omissions, for example no access policy or unclear indication of samples included	12
1* Basic information only (including contact information)	9
U No useful information	2

Figure 2: Suggested minimum data to be included in publicly available information about RTBs.

1. Is the collection for local use only? If yes, no further information is required
2. If applications can be made from external groups does this include:
   a. applications from outside the UK?
   b. commercial entities? (If yes, are any excluded, e.g. tobacco companies?)
3. How will applications be assessed?
   a. biobank manager or management group?
   b. independent assessment by individuals or a panel?
4. Will a separate ethics application be required, or can a request be made to include it under an existing ethics approval held by the biobank?
5. Will any charges be made to assess samples to recover costs? If so, what items of service will be included?
6. Approximately how long will it take to assess an application and provide samples?
7. Contact details

pull out the information relevant to applications was not related to the aesthetic quality or probable cost of the websites. However, sites that included essential information on downloadable documents took significantly longer to assess.

The task of locating samples for use in research would be greatly simplified using a standard checklist for applicants on the UKCRC Tissue Directory and, if available, biobank websites, including the information listed in Figure 2.

In addition, consideration should be given to making the inclusion of this information on the HRA database and UKCRC Tissue Directory mandatory for ethical approval of an RTB, and monitored on a regular basis. These measures should help to maximise the return on investment made by research funders and host institutions in the establishment of RTBs. Most importantly, it will help tissue donors and researchers to accelerate the rate of progress in the discovery of new ways to diagnose and treat cancer.

References at www.rcpath.org/bulletin-apr19

Professor Andrew G Hall, Professor Valerie Speirs, Dr Jane Hair, Professor Gareth J Thomas on behalf of the National Cancer Research Institute's Cellular Molecular Pathology Initiative

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Genetic haemochromatosis to have an all party parliamentary group

The days may well be numbered before genetic haemochromatosis (GH) loses its unwanted reputation for being 'the most common condition you have never heard of'. Read on to see how its profile is about to rise.

Most patients diagnosed with GH confess to never having heard of the condition. Indeed, even many doctors and healthcare professionals remain unaware of the high prevalence of the GH gene (*HFE*) among those in our population of North European and particularly Celtic extraction. Among these populations, one in eight are heterozygous carriers and about one in 200 are homozygous for the C282Y mutation in the *HFE* gene.

The *HFE* gene was first described in 1996.[1] C282Y homozygotes are at risk of excessive iron absorption from the gastrointestinal (GI) tract and excessive iron release from the reticuloendothelial iron stores. The body has no physiological mechanism to excrete excess iron. As iron accumulates, serum ferritin and serum iron levels rise. As plasma iron rises, it saturates its carrier protein transferrin, leading to parenchymal iron overload and toxicity. While serum ferritin reflects the total iron burden, transferrin saturation reflects the potential for end organ damage. This toxicity mostly affects the liver, pancreas, joints and skin. Indeed, it is iron toxicity in the pancreas and skin that gives rise to 'bronze diabetes' as the moniker for GH.

Despite the genetic advances made in the past 20 years, it is not known why some homozygotes develop severe iron overload and end organ