

Biobank development

In an illuminating interview, **Professor William Ollier** and **Dr Martin Yuille** outline how biobanks are becoming an increasingly important means of collecting, storing and distributing biological samples



Can you define the term 'biobanking' and outline some of its applications?

WO&MY: A biobank comprises the facilities and expertise required for the proper management of biological samples, which allow those samples to be effectively collected, processed, stored, distributed and linked with other types of data. Biobanks exist for human, animal, plant and microbial samples, and are most frequently funded to facilitate biomedical research; however, they increasingly serve to support therapeutic interventions as well. Following the sequencing of the human genome, biobanking has expanded enormously to facilitate large-scale genetic and epidemiological studies and to understand how genes, environments and lifestyles contribute to health and disease.

What was the scientific context in which the Centre for Integrated Genomic Medical Research (CIGMR) and the UK DNA Banking Network were initiated?

WO&MY: CIGMR was founded in 2002, shortly after the international Human Genome Project had described the sequence of all the human chromosomes. CIGMR was one part of the attempt to explore how this sequence could be used to obtain meaningful benefits for humankind. Funding for the Centre initially came from the Medical Research Council (MRC) as part of a significant investment package into the science base of Northwest England in the UK. MRC also had the foresight to recognise that future genetic and genomic experiments would require large numbers of well-

characterised clinical samples from across the range of common, high-impact diseases. This led to the funding, in 2000, of 14 consortia of clinicians and researchers, followed in 2003 by funding of a UK DNA biobanking network where samples would be processed, stored and distributed. The original MRC DNA Bank comprised three centres working in partnership across the UK: CIGMR at the University of Manchester, the MRC Human Genome Mapping Project (HGMP) Resource Centre on the Hinxton Genome Campus and the European Cell and Culture Collection (ECACC) in Salisbury.

This arrangement changed when MRC closed its Resource Centre in 2005. Closure required all DNA samples to be transferred and managed in Manchester; and the infrastructure was renamed the UK DNA Banking Network. A few years later, MRC sought further change involving transfer of all related cell lines from Salisbury to Manchester; resulting in a network comprising a centralised biobank plus largely informal contact with the 14 disease consortia.

Can you outline your own scientific backgrounds, and how you are involved with these operations?

WO: I am an immunologist by training and from early on in my career I focused on the genetic control of immune responses and their relevance to tissue rejection, inflammation and autoimmunity. I became fascinated by the human leukocyte antigen (HLA) system and its association with disease susceptibility. Through this, I developed an interest in non-Mendelian common complex human conditions – such as musculoskeletal conditions – which eventually led me to study genetic epidemiology. One role that I have specifically played is to position our activities in a broader international framework with Public Population Projects in Genomics (P3G) and other major initiatives around the world.

MY: I am a molecular geneticist, and my initial research was in microbial systems and

subsequently human oncology. My interest in biobanking started when I worked for the MRC's Resource Centre outside Cambridge and began to recognise the special importance of research infrastructure to postgenomic science. In Manchester, I became Associate Coordinator of the European biobank network project (Biobanking and BioMedical Resources Infrastructure – BBMRI) that is now coming to fruition.

What role has IT played in the UK DNA Biobanking Network project?

WO&MY: It would be impossible to track the 600,000 plus tubes in our biobank without the use of IT; specifically a customised laboratory information management system (LIMS). By using this, alongside robotics, we have levels of accuracy in sample handling that would otherwise be unachievable. Use of web-based LIMS has allowed us to work with a second biobank, providing it with the same levels of efficiency and accuracy at marginal cost. By combining data from the LIMS with web-based tools, we publicise the material, data and studies on diseases without compromising security or privacy.

Have there been analogous projects in other parts of the world?

WO&MY: An international biobank network is currently under construction across Europe. This network (BBMRI-ERIC) aims to link together national networks in Member States and Associated States. Such networks are maturing in Austria, Czech Republic, Estonia, Finland, France, Germany, Greece, Italy, Latvia, Malta, Norway, Sweden, Spain and The Netherlands. Other nations, such as the UK, Ireland and Poland, are at an earlier stage of network development.

Major biobank initiatives are ongoing in most OECD countries, in line with OECD recommendations issued in 2001. As well as our EU links, CIGMR has relationships with initiatives in Japan, Canada, Taiwan, Saudi Arabia, Qatar, Abu Dhabi and the US.

A good investment

Researchers based in the Centre for Integrated Genomic Medical Research at the **University of Manchester**, UK, have built expertise regarding the storage and distribution of human biological samples and data for advancing translational research

SINCE THE COMPLETION of the Human Genome Project in 2001, it has become possible to find variation in the genetic code that contributes risk to the development of specific diseases, or else identify why some people respond badly to a particular drug. However, before these findings can be translated to the clinic, researchers require an ever-increasing number of cases for genetic and other comparisons, necessitating closer worldwide collaboration between researchers and clinicians. The task of aggregating and managing access to biological samples and accompanying clinical data is being undertaken using an innovative medical tool termed a biobank.

Not only are biobanks repositories for processing, storing and distributing biological samples, they also facilitate the centralisation of data management. Researchers can then have controlled access to data on tens or hundreds of thousands of individuals, saving money and quickening the pace of research. Crucially, biobanks have also paved the way for genome-wide association studies and other tests that enable scientists to identify disease biomarkers.

William Ollier, Professor of Immunogenetics and Dr Martin Yuille, Reader in Biobanking, both based at the University of Manchester, UK, are co-Directors of the Centre for Integrated Genomic Medical Research (CIGMR), and have extensive expertise in biobank research. Over the past 10 years, Ollier has largely focused on exploring the genetic basis of common complex disorders, such as rheumatic diseases and autoimmune conditions. Yuille, meanwhile, has been involved with developing biobanking infrastructure across Europe and approaches and policies for sharing data and samples. CIGMR manages 250,000 samples in total and until recently this incorporated the Medical Research Council (MRC) UK DNA Banking Network (UDBN).

UK DNA BANKING NETWORK

The biobanking section of CIGMR is a 13-member team comprised of academics,

project managers, IT specialists and technicians. The aim of this group is to facilitate translational medicine by supporting projects that collect, store and distribute biological samples and associated data for research purposes. One of the most notable projects it has been involved with over the past 10 years is the UDBN. Funded by the MRC and launched in 2003, the purpose of the UDBN was to apply cutting-edge epidemiological approaches to research into common human diseases. This was achieved by providing the scientific community with access to high-quality DNA samples and data, designing new methodologies for improving biobank science and attempting to advance UK science more generally through practical support and the dissemination of knowledge.

As a secondary biobank, the UDBN aggregated and managed resources originated by other biobanks. The Network consisted of clinician-led investigation groups – each specialising in a specific disease – and a research infrastructure to manage the samples and data. Importantly, secondary biobanks manage all data and samples in a standardised way, resulting in a structuring effect on research and accelerated progress in genetic epidemiological studies. By the completion of the UDBN project in 2013, it had played a key role in preparing samples for a significant proportion of the diseases included in the genome-wide association studies that formed the Wellcome Trust Case Control Consortium. It had also helped to inform the technical development and testing of protocols and automated processes of the UK Biobank project – a major national prospective study that has recruited 500,000 people aged 40–69 to investigate the role of lifestyle, genes and environment in the development of particular diseases.

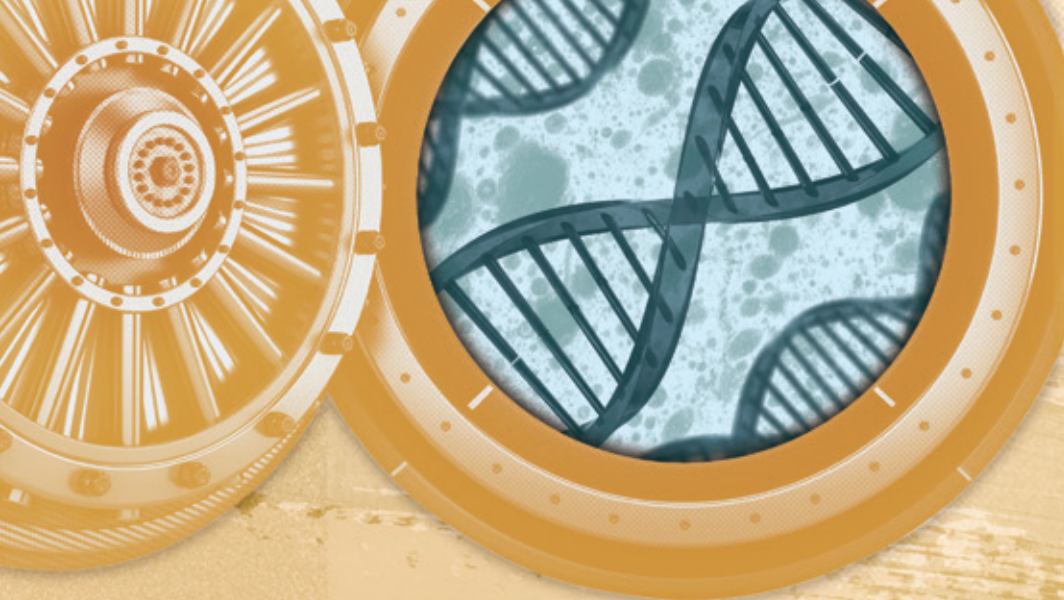
Alongside its extensive achievements, however, the UDBN also faced significant challenges. For example, lack of long-term planning from some of the agencies involved, and shifts in the priorities of the funder

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following successive changes in its executive leadership, resulted in inconsistency in its assessment of the importance of the venture and its long-term value. Additionally, while the MRC and other funders wanted to promote an 'open access' data model, the clinical consortia collecting and submitting material struggled to agree to this, leading instead to the development of an alternative and pragmatic 'fair access' model. Perhaps most importantly, Ollier and Yuille faced difficulties in convincing funders that investing resources into improving the quality and efficiency of sample collection, preparation and storage would confer enormous advantages for future scientific output.

FORGING AHEAD

Even after the discontinuation of the MRC UDBN, a number of the original MRC-funded collecting consortia still use CIGMR to manage and distribute their samples to collaborating groups. In fact, the CIGMR biobanking facility has continued to thrive, attracting other large projects such as the Motor Neurone Disease Association's national sample collection. At present, the CIGMR team is developing biobank facilities with common capabilities throughout the region of Greater Manchester. In an exciting move, the researchers have partnered with Salford Royal NHS Foundation Trust and Salford Care Commissioning Group in order to build infrastructure that enables the collection of biological samples from different



INTELLIGENCE

CENTRE FOR INTEGRATED GENOMIC MEDICAL RESEARCH (CIGMR) BIOBANKING: SUCCESSES AND FUTURE DIRECTIONS

OBJECTIVES

- To develop high quality biological samples linked with extensive clinical, lifestyle and demographic data for important human health conditions
- To maximise clinical research efforts in important human diseases by providing the best scientists with the best epidemiological datasets
- To avoid duplication of sample and data collection and in so doing save funding that can be used for increased research activity

PARTNERS

University of Manchester, UK • Manchester Academic Health Science Centre, UK • Salford Royal NHS Foundation Trust, UK • UK Biobank • Motor Neurone Disease Association • Arthritis Research UK • EU and Innovative Medicines Initiative (IMI) projects

FUNDING

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MARTIN YUILLE is Reader in Biobanking at the University of Manchester. He was Associate Coordinator of Biobanking and BioMedical Resources Infrastructure and has provided advice on biobanking to the governments of France, Germany, Japan and Poland.

clinical conditions and longitudinal electronic health record data. Importantly, the structure of Salford's health system is progressive and forward-looking: "Highly detailed and integrated records exist for approximately 240,000 residents with now 14 years of longitudinal follow-up," Ollier discloses. "When combined with appropriate biological samples, this represents a powerful resource for investigating how genetic, environmental and lifestyle risk factors contribute to disease susceptibility, progression and outcome – and could provide a valuable parallel resource to sit alongside the UK Biobank."

The researchers at CIGMR are also exploring the possibility of integrating other clinical- and environment-related databases into their existing health databases. Their ultimate goal is to create a 'living laboratory' in Salford, whereby scientific research translates into the improvement of the residents' health and quality of life. In order to achieve this, Ollier and his team are working alongside the Salford Citizen Scientist project in order to conduct detailed consultations with the target population that ensure such an initiative would benefit from public support and participation.

FUTURE INVESTMENTS

Crucially, the MRC has recently announced its decision to partner with other funders to invest once more in the national coordination of biological samples in the UK. The proposed initiative aims to create a searchable national catalogue of the collections that exist in the UK, including specific information regarding custodians, samples and data. It also aims to advance the standardisation of biobank protocols and processes, and to improve coordination between biobanks. The hope is that this project will be an important step forward in health-related research in the UK. Additionally, the National Institute for Health Research (NIHR) is currently funding the development of more UK Biocentre sites in both Milton Keynes and Leicester, representing partnerships with

the University of Oxford and other London Academic Health Science Centres.

Despite the proven utility of the UK Biobank project, there is still a need for more case-control biobank collections for less common diseases that include individuals outside the 40-69 age range. Alongside this, it is also vital that the biological samples and accompanying data from patients are kept safe and accessible, and that they are treated as a valuable resource for the advancement of medical research.

THE NETWORK'S IMPACT

Some of the UK DNA Banking Network's notable successes included:

- Distributing over 180,000 samples of DNA to investigators
- Facilitating a large number of research projects and their publication
- Becoming the first academic research biobanking structure in Europe to introduce an ISO 9001 quality management system
- Acting as a major advisor and test bed for the sample management component of UK Biobank
- Providing trained staff for UK Biobank and other centres in the UK
- Publishing a significant number of peer-reviewed papers on biobanking methodology, policy and strategy
- Holding annual international biobanking training workshops that were well-attended by researchers from across the EU and elsewhere