

BIORESOURCE PAPER

# The Northern Ireland Biobank: A Cancer Focused Repository of Science

Claire Lewis<sup>1</sup>, Stephen McQuaid<sup>1</sup>, Priscilla Clark<sup>1</sup>, Paul Murray<sup>1</sup>, Tracey McGuigan<sup>1</sup>, Christine Greene<sup>1</sup>, Bronagh Coulter<sup>1</sup>, Ken Mills<sup>2</sup> and Jacqueline James<sup>1</sup>

<sup>1</sup> The Northern Ireland Biobank, Centre for Cancer Research and Cell Biology, Queen's University Belfast, UK

<sup>2</sup> Centre for Cancer Research and Cell Biology, Queen's University Belfast, UK

Corresponding author: Claire Lewis ([claire.lewis@qub.ac.uk](mailto:claire.lewis@qub.ac.uk))

The Northern Ireland Biobank (NIB) was established in 2011 as a joint initiative between Queen's University Belfast and Belfast Health and Social Care Trust to provide the infrastructure for the standardised collection and storage of high quality, well annotated human tissue samples, with matched bloods and bodily fluids to underpin cancer research in Northern Ireland and beyond. The NIB has been instrumental in supporting translational research locally, nationally and internationally with a number of key achievements to date. The vision of NIB is to develop an internationally recognised biobank network within Northern Ireland which collects, stores and distributes high quality, clinically annotated biospecimens for biomarker research to benefit cancer patients.

**Keywords:** Biobank; Tissue Bank; Biological Samples; Cancer; Bioresource; Biospecimens

**Funding statement:** NIB receives core funding from the Health and Social Care Research and Development Division of the Public Health Agency in Northern Ireland with charitable funding from Friends of the Cancer Centre. NIB previously received charitable funding from Cancer Research UK and Prostate Cancer UK.

## (1) Bioresource Overview

### Project description

The Northern Ireland Biobank (NIB) is currently a disease specific biobank and was awarded full ethical approval in August 2011 for the collection of tumour and non-tumour control tissues and associated biospecimens from patients with a suspected or confirmed diagnosis of cancer [1]. The NIB prospective collection targets colorectal, breast, prostate, gynaecological, lung, head and neck and haematological malignancies with linkage to robust de-identified clinico-pathological data. Donation is voluntary and requires written informed consent from patients in accordance with the Human Tissue Act (2004). Tissue sampled for NIB is always surplus to clinical need to ensure that patient diagnostics are not compromised.

NIB's status as a fully ethically approved tissue bank offers substantial benefits for researchers who apply to use tissue procured by NIB. Subject to an application and scientific peer review process, NIB's ethical approval extends to UK studies receiving non-identifiable tissue and data from the bank; eliminating the need for individual project based ethical approval. NIB have a straightforward application system based on the UK's Integrated Research Application System with efficient turnaround times, thus offering a significant advantage to researchers who are

have traditionally faced lengthy delays when applying for individual project based approvals from local research ethics committees.

Key achievements of the NIB to date include:

- A rigorous regulatory framework which complies with research ethics and governance requirements for handling of human biospecimens for research. This provides timely release of samples to researchers with scientifically approved projects.
- Approval to utilise local NHS tissue pathology formalin fixed paraffin embedded (FFPE) archive material to establish a series of 'retrospective' collections.
- The creation of novel resources including DNA libraries and custom-built tissue microarrays from defined cohorts of FFPE tissues relocated to the NIB from the BHSC pathology archives [2].
- Infrastructure to support individual requests from Chief Investigators for specific types of collections including fresh tissues for explant culture.
- A robust quality management system with regular audit across all aspects of NIB workflow.

NIB has been instrumental in providing the core infrastructure and tissue access that has been critical to successfully leveraging major external grant funding to

support translational research in Northern Ireland. NIB has also been instrumental in improving the quality and impact of research generated within the NI cancer research community [3–6]. This is reflected in the increased peer reviewed, high impact factored publications which have relied on NIB resources. Collaborations with local industry have also been forged through improved access to quality assured clinical samples. One NIB application made by Almac Diagnostics has contributed to the development of an assay to assess chemotherapy response in Breast Cancer. This research was published in the Journal of the National Cancer Institute and acknowledges the support given by the NIB [7].

### Classification (1)

Human

### Species

Human

### Classification (2)

Biological samples and associated data.

### Context

#### *Spatial coverage*

Centre for Cancer Research and Cell Biology, Belfast, Northern Ireland, United Kingdom.

Latitude: 54.585997

Longitude: -5.944160

#### *Temporal coverage*

NIB consent and sample collection commenced in November 2011. There is no indicated end date.

#### *Temporal coverage for accessibility*

N/A

## (2) Methods

### Steps

#### *NIB prospective collection from patients with solid tumour malignancies*

NIB support a prospective collection of human biospecimens from patients with solid tumour malignancies including: fresh and FFPE tumour and normal tissue; whole blood; plasma; serum; buffy coat; urine; saliva; bodily fluids such as ascites or pleural fluid. The workflows associated with this collection are as follows:

1. NIB Clinical Research Nurses (CRN) or NIB Technician liaise with the relevant clinical teams to identify patients with a suspected or confirmed diagnosis of cancer who are suitable for donation.
2. Patients are approached by NIB CRN or Technician and informed consent is sought.
3. Prior to surgery, NIB collect blood and other bodily fluids where appropriate.
4. Bloods are processed into their derivatives according to NIB Standard Operating Procedures (SOPs) and placed into dedicated NIB storage.

5. Fresh tumour and normal tissue and FFPE is acquired through the local NHS tissue pathology laboratories. Where fresh tissue is to be collected, the specimen is brought fresh to the pathology laboratory for sampling by a Histopathologist or Advanced Biomedical Scientist trained in dissection. On lesser occasions, tissue may be sampled in theatre under direction of a Consultant Pathologist. Fresh tissue is immediately snap frozen following sampling.
6. The case is reviewed a Consultant Histopathologist who allocates two FFPE tumour blocks and two FFPE normal blocks to NIB.
7. Consent, sample collection, metadata and storage locations are all captured in the NIB's Information Management System.
8. NIB Biomedical Scientist or NIB Technician undertake tissue sectioning and nucleic acid extractions depending on study requests. Where a request has been made for FFPE tissue, NIB only release tissue sections to maximise future use of the parent block. Likewise, aliquots of blood/blood derivatives are made available dependent on the volume required by the study.
9. Matched de-identified clinic-pathological data is provided to the researcher upon study approval (for further information, see 'source of associated data' below).

#### *NIB prospective collection from patients with haematological malignancies*

NIB supports a prospective collection of biospecimens from patients with haematological malignancies including peripheral whole blood and bone marrow tissue. The workflows associated with this collection are as follows:

1. Patients are approached by a haematology clinician and informed consent is sought.
2. Peripheral whole blood and bone marrow is obtained by the haematology clinician for diagnostic assessment. Any material surplus to diagnostic use will be donated to NIB.
3. Peripheral whole blood and bone marrow samples are processed according to NIB Standard Operating Procedures (SOPs) and placed into dedicated NIB storage facilities.

#### *NIB retrospective collection*

Retrieval of large cohorts of FFPE cancer tissues from the NHS diagnostic pathology archives has facilitated the creation of a unique set of resources for the NIB referred to as the 'NIB retrospective collection'. With over 15,000 samples pulled from the archives to date, these samples have been used in specific study requests, to custom build tissue microarrays (TMAs) and to create DNA libraries. The retrospective samples are enhanced by linkage with robust clinical and pathological data acquired from the Northern Ireland Cancer Registry. The blocks are retained in the secure NIB storage area but can be returned immediately to the parent trust if required for further diagnostic testing. Tissue blocks are only sectioned by trained and

experienced NIB staff. All staff performing microtomy have received competency training, work to SOPs which includes instruction to always leave tissue on the block.

### Stabilization/preservation

A variety of stabilization methods are utilised by NIB:

- FFPE tissue: Tissue is placed in 10% neutral buffered formalin until processed.
- Fresh tissue: Following sampling, fresh tissue is snap frozen in liquid nitrogen or pre-cooled isopentane. On request, fresh tissue can also be placed directly into media.
- Whole Blood, buffy coat and plasma: collected in Ethylenediaminetetraacetic acid (EDTA) tubes.
- Serum: collected in a Serum Clot Activator tube.
- Bone Marrow: collected in EDTA tubes.
- For specific study requests NIB can facilitate the collection of blood using tubes with stabilizing agents eg PAXgene tubes; Streck tubes.
- For specific study requests NIB can facilitate the collection and immediate distribution of bodily fluids such as ascites or pleural fluid.

### Type of long-term preservation

FFPE blocks and slides are stored at room temperature in a manual storage unit. Fresh frozen tissues and blood samples are stored at  $-80^{\circ}\text{C}$ ; DNA aliquots are stored at  $-20^{\circ}\text{C}$ . Viable cells from bone Marrow samples are stored in liquid nitrogen units ( $-196^{\circ}\text{C}$ )

All samples are individually labelled with a unique sample identifier to ensure donor anonymity and are stored in a dedicated NIB storage facility. This facility has restricted access with remote wireless monitoring of room humidity, room temperature, voltage and individual freezer temperatures. An automated alert system warns NIB staff via telephone, email and text message of variation from pre-set operating parameters.

### Storage temperature

FFPE blocks, slides and TMAs are stored at room temperature. Fresh frozen tissue and aliquots of serum, plasma, whole blood and buffy coat are all stored at  $-80^{\circ}\text{C}$ . DNA is stored at  $-20^{\circ}\text{C}$ .

### Shipping temperature from patient/source to preservation or research use

Ambient temperature.

### Shipping temperature from storage to research use

Frozen samples (tissue and/or blood derivatives) are shipped on dry ice. FFPE blocks and slides are transferred at ambient temperature.

### Quality assurance measures

NIB operates a quality management system (QMS) to achieve continual quality improvement. Key aspects of the NIB QMS include:

- A dedicated lead for Quality Management who oversees the QMS.

- A rigorous set of SOPs for the collection, processing, storage and distribution of human tissue and associated biospecimens. SOPs are based on best practice guidelines and/or best available evidence.
- Risk Assessments for the tissue and tissue handler.
- Staff induction, training and competency assessment to ensure staff are trained and competent in the skills specific to their job.
- Horizontal and vertical internal audits; participation in external quality assurance programs such as the Integrated Biobank of Luxembourg Proficiency Testing Scheme.
- All tissue is sampled and processed in a UKAS accredited NHS tissue pathology laboratory (ISO 15189 Medical Laboratory Accreditation).
- Pathological review of tissue including % tumour; nucleic acid qualification and quantification including RIN/Qubit/Nanodrop where needed.
- A NIB Steering Committee meets at least twice a year to oversee the good practices of the NIB on an ongoing basis.

### Source of associated data

More commonly, NIB acquire de-identified clinico-pathological data from the Northern Ireland Cancer Registry (NICR). For each cancer type, NIB have developed core datasets which include long term follow up data where available. An example a dataset for lung cancer will include anonymised information on family history, smoking history, co-morbidities, overall stage, surgery and treatment details as well as recurrence information. NIB currently fund a full time member of staff who sits within the NICR to facilitate data linkage.

Data which is not available from the cancer registry may also be extracted for specific studies by clinicians or NIB NHS employed research nurses/technicians under the ethical approval granted to a particular study. Patients are not required to complete a data questionnaire at the time of consent or sample acquisition.

All data released to NIB approved studies is de-identified and linked to a unique code number at source; NIB never release data which contains information which could identify an individual.

### Ethics Statement

NIB is a Health and Social Care Research Ethics Committee approved tissue bank. NIB were first awarded ethical approval by the Office of Research Ethics Northern Ireland (ORECNI) for the consent, collection, storage and distribution of human tissue samples and associated data in March 2011 (OREC reference: 11/NI/0013). This approval was granted for five years and was renewed in 2016 (OREC reference 16/NI/0030).

NIB operate under the Queen's University Belfast Human Tissue Authority Research License (MBC/BCH Research Licence 12044) for the removal, storage and use of human tissue for research.

NIB has generic and enduring ethics approval which enables researchers to use samples from the NIB prospective collection as long as the research falls within the remit of the NIB ethics approval. The ethics covers a wide variety

of research areas and tests. There are restrictions however on the use of tissues from the diagnostic tissue pathology archives. For example, studies wishing to undertake whole genome sequencing of samples from the pathology archives will be required to obtain independent ethical approval. Studies where there is an intention to link the results to specific patient identifiers (family names etc) will not be supported by NIB.

### Constraints

Currently NIB only consent donors who are receiving care in the Belfast Health and Social Care Trust.

## (3) Bioresource description

### Object name

Cancer

### Bioresource name

The Northern Ireland Biobank

Bioresource acronym: NIB

### Bioresource location

NIB is located within the Centre for Cancer Research and Cell Biology in Queen's University Belfast. Patient consent and sample collection occurs within the Belfast Health and Social Care Trust. NIB currently have access to the tissue pathology archives of three of the four pathology departments in Northern Ireland.

Northern Ireland Biobank  
Queen's University Belfast  
Centre for Cancer Research and Cell Biology  
97 Lisburn Road  
Belfast  
BT9 7AE

### Bioresource contact

NIB Administrator:

Tel: 028 90972915

Email: [nibiobank@qub.ac.uk](mailto:nibiobank@qub.ac.uk)

### Bioresource URL

<http://www.nibiobank.org/>

### Identifier used

<http://www.nibiobank.org/>

### Bioresource type

Cancer

### Type of sampling

Disease based sampling

### Anatomical site

NIB support targeted prospective collections in the following cancer types:

- Colorectal

- Breast
- Prostate
- Gynaecology
- Head and Neck
- Lung
- Haematological malignancies

NIB can facilitate the retrieval of FFPE tissue blocks for all cancer types from diagnostic tissue pathology archives in Northern Ireland. See **Table 1** for further information on the types of biospecimens collected by NIB.

### Disease status of patients/source

Cancer

### Clinical characteristics of patients/source

NIB consent both male and female patients who are over 18 year of age with no upper age restriction. Patients must have a suspected or confirmed diagnosis of cancer and be able to provide informed consent. For the solid tumour prospective collection, blood samples (and urine or saliva if appropriate) are collected pre-surgery with tissue sampled from the surgical resection specimen. For the haematological prospective collection, blood and bone marrow samples are collected at the time of initial investigation for cancer.

On request, NIB can also facilitate additional collection of blood samples, bodily fluids or tissue which is surplus to diagnostic need. For example, longitudinal collection of plasma for ctDNA analysis at time points during cancer treatment to determine response to therapy.

NIB's access to diagnostic tissue pathology archives allows for retrieval of FFPE cohorts with varying clinical characteristics. NIB can facilitate retrieval of diagnostic biopsies and resection tissue as well as metastatic tissue.

### Size of the bioresource

NIB have prospectively consented >2770 donors and have accumulated over 90,000 samples as of February 2018. The average annual recruitment is 462 donors per year.

As of February 2018, NIB have received 238 applications with over 40,350 samples released approved applications.

Recruitment and collection of biospecimens is ongoing with no indicated end date.

### Vital state of patients/source

Alive

### Clinical diagnosis of patients/source

Cancer

### Pathology diagnosis

Variable across different cancer types and subtypes

### Control samples

NIB routinely collect matched non-tumour control fresh and FFPE tissue from the donor resection specimen.

**Biospecimen type****Table 1:** Overview of the types and numbers of samples collected by NIB.

Biospecimen	Number of Aliquots/Blocks	Volume/ Size
Whole Blood	3	1 ml
Plasma	3	1 ml
Buffy Coat	1	N/A
Serum	2	1 ml
Urine	10	1 ml
Saliva	1	N/A
Fresh Frozen (tumour)	2	~0.5 mm <sup>3</sup>
Fresh Frozen (normal)	2	~0.5 mm <sup>3</sup>
FFPE (tumour)	2	N/A
FFPE (normal)	2	N/A
Bone Marrow	Variable	Variable
Bodily fluids (ascites; pleural fluid)	On request	On request

**Release date**

N/A

**Access criteria**

Applications for NIB samples can be made by Chief Investigators from academia and healthcare that are internal and external to Northern Ireland. NIB also welcome industrial/commercial applications.

To access samples, Chief Investigators (CI) must complete an electronic preliminary application via the NIB website. Details required in this preliminary application include a scientific abstract, details of the Chief Investigator and Co-Investigators, source of funding, and the number and type of samples required. The purpose of the preliminary application is to:

- Allow NIB to determine if the study falls within the remit of NIB's ethical approval;
- The required sample set is available within a realistic time-frame;
- There is evidence of sufficient funding to carry out the research.

The CI may be asked to pursue additional ethics approval should the study be deemed to fall outside of the remit of the NIB ethics approval. Following NIB internal review of the preliminary application the researcher will be asked to complete a full application and submit it with a detailed scientific protocol.

Applications are reviewed by two reviewers selected from the NIB Scientific Review Committee which comprises Consultant Histopathologists, clinicians, surgeons and basic scientists. Reviewers will complete a scientific review form which considers:

- Novelty
- Significance
- Study Design
- Research team and facilities
- Value for money

Based on the recommendations of the reviewers and any other project logistics and operational issues, the NIB Senior Team will either approve or reject the application. If the application is approved the applicant will receive formal NIB ethical approval. Chief Investigators must complete a Material Transfer Agreement before release of samples.

NIB's access policy can be found on the NIB website: [www.nibiobank.org](http://www.nibiobank.org).

**(4) Reuse potential**

NIB aliquot liquid samples so multiple samples will be available from the same donor to maximise sample use. Tissue sections or DNA/RNA aliquots from FFPE are distributed to research studies to ensure the block is available for future use. All sample metadata and associated donor clinico-pathological data is retained by NIB for use in other studies. NIB do not request the return of samples that have been distributed to research studies.

**Acknowledgements**

Belfast Health and Social Care Trust Cellular Pathology Department  
Northern Ireland Cancer Registry

**Competing Interests**

The authors have no competing interests to declare.

**Author Roles**

Claire Lewis, Bioresource Manager  
Stephen McQuaid, Bioresource Deputy Director  
Priscilla Clark, Bioresource Administrator  
Paul Murray, Bioresource Clinical Research Nurse  
Tracey McGuigan, Bioresource Clinical Research Nurse  
Christine Greene, Bioresource Biomedical Scientist  
Bronagh Coulter, Bioresource Senior Technician  
Ken Mills, Professor of Experimental Haematology  
Jacqueline James, Bioresource Director

**References**

1. Lewis, C, O'Donnell, A, McQuaid, S and James, J. 2015. Contribution of biobanks to care services. *Cancer Nursing Practice*, 14(9): 21–24. DOI: <https://doi.org/10.7748/cnp.14.9.21.s19>
2. Lewis, C, McQuaid, S, Hamilton, P, Salto-Tellez, M, McArt, D and James, J. 2016. Building a 'Repository of Science': The importance of integrating biobanks within molecular pathology programmes. *European Journal of Cancer*, 67: 191–199. DOI: <https://doi.org/10.1016/j.ejca.2016.08.009>
3. Jain, S, Lyons, C, Walker, S, McQuaid, S, Hynes, S, Mitchell, D, et al. 2017. Validation of a Metastatic Assay using biopsies to improve risk stratification in patients with prostate cancer treated with radical radiotherapy.

- tion therapy. *Annals of Oncology*, 29(1): 215–222. DOI: <https://doi.org/10.1093/annonc/mdx637>
4. **Buckley, N, Boyle, D, McArt, D, Irwin, G, Harkin, D, Lioe, T** et al. 2015. Molecular classification of non-invasive breast lesions for personalised therapy and chemoprevention. *Oncotarget*, 6(41). DOI: <https://doi.org/10.18632/oncotarget.6525>
  5. **Alvi, M, McArt, D, Kelly, P, Fuchs, M, Alderdice, M, McCabe, C** et al. 2015. Comprehensive molecular pathology analysis of small bowel adenocarcinoma reveals novel targets with potential for clinical utility. *Oncotarget*, 6(25). DOI: <https://doi.org/10.18632/oncotarget.4576>
  6. **Bingham, V, McIlreavey, L, Greene, C, O'Doherty, E, Clarke, R, Craig, S** et al. 2017. RNAscope in situ hybridization confirms mRNA integrity in formalin-fixed, paraffin-embedded cancer tissue samples. *Oncotarget*, 8: 93392–93403 DOI: <https://doi.org/10.18632/oncotarget.21851>
  7. **Mulligan, J, Hill, L, Deharo, S, Irwin, G, Boyle, D, Keating, K** et al. 2014. Identification and Validation of an Anthracycline/Cyclophosphamide–Based Chemotherapy Response Assay in Breast Cancer. *JNCI: Journal of the National Cancer Institute*, 106(1). DOI: <https://doi.org/10.1093/jnci/djt335>

**How to cite this article:** Lewis, C, McQuaid, S, Clark, P, Murray, P, McGuigan, T, Greene, C, Coulter, B, Mills, K and James, J. 2018. The Northern Ireland Biobank: A Cancer Focused Repository of Science. *Open Journal of Bioresources*, 5: 9, DOI: <https://doi.org/10.5334/ojb.47>

**Published:** 11 September 2018

**Copyright:** © 2018 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See <http://creativecommons.org/licenses/by/4.0/>.