

BIORESOURCE PAPER

The Tumour Bank at the Children's Hospital at Westmead: An Australian Paediatric Cancer Biorepository

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The Tumour Bank at The Children's Hospital at Westmead was established in 1998 with the purpose of facilitating research into childhood malignancy through the active provision of well annotated, ethically collected tissue samples and providing a pathway for the Children Hospital at Westmead to engage in leading research initiatives, supporting international investigations and clinical trials. Within 20 years practice as a single institute biorepository, The Tumour Bank has established standard operating procedures for collection of tissue, blood and bone marrow that were integrated into routine patient management systems. In addition, three main operational areas have been developed: collection of biospecimens and written consent; management of clinical data and biospecimen inventory database; and implementation of an open access policy to support childhood cancer research around the world. Regulatory oversight is provided by the Tumour Bank Committee, Human Research Ethics Committee and Governance Department. This concerted effort has resulted in collecting 20340 specimens from 3788 patients within 20 years, and The Tumour bank has supported over 108 national and international research projects, and contributed to over 70 peer-reviewed publications to date, with a mean time-to-publication of 19.1 ± 9.0 months and average Impact Factor of 6.11 ± 4.53 . In conclusion, the Children's Hospital at Westmead Tumour Bank has demonstrated a sustained single institutional biorepository model for facilitating translational research of rare cancer. It has provided strong evidence that integration of a single institutional biobank into standard clinical practices would be the long-term pathway of valuable bio-resource for rare cancer research.

Keywords: Tumour Bank; Paediatric cancers; biobanking; translational research; paediatric biospecimen; childhood malignancy

(1) Bioresource Overview

Project description

Paediatric cancers, as rare diseases, require long term collection strategies to ensure comprehensive accrual rates. Paediatric research has been hampered for years due to the lack of quality paediatric biospecimen, and biobanking is the only economical and efficient solution to meet future research needs.

The Children Hospital at Westmead (CHW) is the largest paediatric healthcare centre in NSW, Australia with its Oncology Department treating an average of 150 new patients each year. To support paediatric research, its Tumour Bank CHWTB was founded in 1998 with benefactor funds donated to CHW oncology departments. Presently CHWTB is partly funded by core health funding, research infrastructure grants and benefactors [1]. As a single institution biorepository being embedded in hospital clinical pathways, CHWTB collects residual to diagnostic requirements from all the cancer patients.

CHWTB is closely linked to the primary tissue collection point in the pathology department, which minimises the daily operational cost and ensures consistency and efficiency of practice.

The purpose of the CHWTB is to open an avenue for CHW to engage in leading translational research initiatives, support international investigations and clinical trials, and most importantly promote paediatric cancer research via the active provision of ethically collected samples with full clinical annotation. Via professional and standardized biobanking activity, CHWTB will improve the deeper understanding of paediatric cancer, which is fundamental to a improved healthcare for children with cancer.

In the 19 years of operation the CHWTB has collected 20340 specimens from 3788 patients. CHWTB has actively pursued researcher groups exploring leading translational research in paediatric cancer and we have since facilitated 108 projects both in Australia and other countries around the world (41% from Australia, 26% from the United States,

7% from the United Kingdom, 4% from New Zealand, 3% from Canada and 19% from the rest of the world), which have generated over 70 publications correspondingly [2]. The average Impact Factor of the publications is 6.11 ± 4.53 .

Classification (1)

Human.

Species

Human.

Classification (2)

Biological samples and associated data.

Context

Spatial coverage

The Tumour Bank at The Children Hospital at Westmead is located within The Children Hospital at Westmead, Westmead, NSW, Australia
Latitude (South): 33.8024°
Longitude (Est): 150.9884°

Temporal coverage

Start from 1998 to present, no end date.

Temporal coverage for accessibility

N/A.

(2) Methods

Operation and Procedures

As an embedded facility within the hospital, the CHWTB can collect resected tumours, biopsies, bone marrow and blood samples via the pathology or haematology departments during the normal course of diagnosis and treatment that are in excess of clinical/diagnostic requirements collection. To ensure consistent and comprehensive collection of specimens, standard operating procedures (SOPs) and interdepartmental pathways for samples have been developed. These SOPs outline CHWTB staff's daily practice and our operational relationships and processes with oncology, surgery, histopathology and haematology departments in CHW [3]. All the SOPs followed the guideline of best practice of ISBER [4].

Informed Consent Management and Ethics Committee Compliance

Being within a public hospital, the management of our consenting practices has been simplified profoundly by allowing consent to occur during routine patient consultation, patient admission for treatment or after a sample has been collected for diagnosis or clinical management. Patients are consented after a diagnosis of cancer has been obtained, which typically means that a biospecimen was obtained for diagnostic testing, the residual of which may be made available to the CHWTB upon donor consent. Our practice allows consent to be sought by registrars, clinical fellows, staff specialists and clinical research associates during the normal course of clinical management of the patients, which has dramatically lessen the impact of different staffing arrangements on

consenting rates. Ideally we seek consent during patient consultation of treatment regimens to be provided. Our consenting SOPs strictly follow paediatric biobank consent guidelines [5] as summarized below:

- Potential donors, their parents or legal guardians must be informed by written documents that the potential intended use of the sample will be for research projects only.
- Parents or legal guardians of children under 12 years of age are asked to make written and broad consent to allow future unspecific studies. However, donors reserve the right to withdraw their specimen at any time.
- Assent from children >12 years of age can be requested and confirmed when deemed appropriate by parent or consentor.
- Whilst it is not yet obligatory to re-consent patients when they have reached the age of majority, that is 18 years and over, the CHWTB may re-consent and remind patients about samples already stored in the biobank as opportunity to do so occurs (eg. During late effects clinics).
- The specimen mustn't be used for any other purpose than valid biomedical research, This excludes applications that are purely commercial in nature.
- Both the specimens and matching clinical data must be de-identified before being released to researchers. In addition to the consideration of protecting donor privacy, confidentiality and cultural sensitivities of children are also considered.

Additional mechanisms have been developed that allow us to seek consent from patients whose consultation regarding donation of tissue to the CHWTB could not be sought during their admission to hospital, This includes use of letters to follow up remote patients or working with bereavement counsellors to seek consent from families where a child may have died.

Research Review and Governance

The researchers must formally apply through the Tumour Bank Committee to access the samples. The Tumour Bank committee will review the scientific feasibility of the project. Evidence of local or institutional human ethics committee approval must be presented with the application prior to the samples release to the applicants. Our current consent form has a tick box where donors can express their wishes with regards to return of the incidental findings. In the event that the committee identifies that incidental findings are likely their return will be specified to the researchers, as our current practice is to notify and transfer the responsibility to a treating clinician to determine further course of action. This is reflected in our Consent form and Patient Information Sheet.

Public Awareness

The consent process CHWTB is also supplemented by the provision the CHWTB "Newsletter" that describes basic processes and research that has been supported by our

samples [6]. CHWTB consents for unspecified research, any future matched blood collection, and serial leukaemia bone marrow samples. CHWTB obtains all samples ethically and written consent has been recorded for all samples.

Data Linkage

Another advantage of being a biobank embedded with the hospital is the clinical data linkage. CHWTB only collects essential data at the collection point and enters into our database. If any specified data is missing at the collection point, it is obtained from the hospital database since the full data access is available, which includes demographic information, laboratory tests, diagnosis, and treatment, etc. All the diagnosis is in ICCC and ICD-O coding for international standardization. In addition, as it is part of the Sydney Children's Hospital Network, the network security can be accomplished by hospital firewall. All the data is de-identified before being released to any researchers.

Stabilization/preservation

- Ethylenediaminetetraacetic acid (EDTA), Acid-Citrate-Dextrose (ACD), RPMI
- Snap freeze tissue in liquid nitrogen

Type of long-term preservation

- Formalin Fixed Paraffin Embedded (FFPE)
- Frozen
- Cryogenic preservation

Storage temperature

- Room temperature (bone marrow smears)
- -20°C (for clinical trial samples)
- -80°C (tissue, blood, bone marrow, cerebrospinal fluid)
- -160°C (cells)

Shipping temperature from patient/source to preservation or research use

Room temperature (18–25°C)

Shipping temperature from storage to research use

- Room temperature (FFPE sections)
- -78°C dry ice (DNA, RNA, blood & Bone marrow)

Quality assurance measures

- SOPs will be followed throughout all the sample collection and processing steps.
- Quality of FFPE tissue will be checked morphologically and immunohistochemically to assure proper tissue processing and fixation and therefore sufficient antigenic preservation.
- The tumour diagnosis (including grading using the most current diagnosis system), percentage of tumour, percentage of stroma, and percentage of necrosis will be assessed by histopathologist.
- DNA will be quantified by nano drop and picogreen.
- DNA&RNA will be checked by Agilent 2100 bioanalyzer.
- Specific biomarkers will be checked according to specific downstream request.
- Compliance with local ethics/governance and national laws, eg. Human Tissue Act (2004) [7].

Source of associated data

Hospital databases—Oncology Patient Register, pathology report, clinical test results, clinical notes, treatment protocols, etc.

Ethics statement

The ethical approval from the CHWTB to meet its stated purpose in supporting national and international research into paediatric cancer through the provision of ethically collected biospecimens has provided by Sydney Children's Hospitals Network Human Research Ethics Committee in New South Wales, Australia. The approval was initiated in 1998, and reviewed every 4 years since.

(3) Bioresource description

Object name

Paediatric cancers.

Biobank name

The Tumour Bank at the Children's Hospital at Westmead.

Bioresource acronym: CHWTB.

Bioresource location

170 Hawkesbury Rd, Westmead, NSW, Australia 2145.

Bioresource contact

Associate Professor Daniel Catchpoole: daniel.catchpoole@health.nsw.gov.au.

Bioresource URL

<https://www.schn.health.nsw.gov.au/health-professionals/statewide-laboratory-services/tumour-bank>.

Identifier used

N/A.

Bioresource type

Paediatric cancers. These include samples collected from leukaemia patients (34%) collected at diagnosis, remission, relapse and during other significant treatment time points, solid tumours available include all cancers that appear in children, the majority being lymphomas (10%), brain tumours (16%), carcinomas (2%), neuroblastomas (8%), sarcomas (10%), liver and kidney tumours (6%), germ cell tumours and other rare tumours (14%).

Type of sampling

Disease based.

Anatomical site

Variable.

Disease status of patients/source

Paediatric cancers.

Clinical characteristics of patients/source

Paediatric tumour samples with full clinical data, de-identified before released to researchers.

Size of the bioresource

3788 patients as at 3/5/2017.

On-going recruitment of ~150 new patients per annum.

Collection is ongoing and has no definite end date.

Vital state of patients/source

Alive/Deceased.

Clinical diagnosis of patients/source

Variable.

Pathology diagnosis

Variable—representing over 50 types and subtypes of paediatric cancers.

Control samples

CHWTB doesn't collect control samples from healthy children. As consent allows, germ line samples (peripheral blood) from the majority of patients with solid tumours have been collected, stored and are used as matched control samples for comparison with tumour tissue.

Biospecimen type

CHWTB provides a different variety of biospecimen including serum, plasma, DNA, RNA, cerebrospinal fluid, fresh frozen tissue, FFPE tissue and Tissue Microarray.

Release date

Open since 1998, applications received from interested researchers.

Access criteria

Via active or passive communication with researcher, the CHWTB will capture the research interest of the researcher and provide them the number and type of samples suitable for the researcher. Researchers request access to the CHWTB sample resource through an application mechanism. Applications need to be accompanied by approval from the researchers' local host ethics committee or governance system, evidence of funding availability to see the project through to completion and a scientifically valid research proposal. The applications are reviewed by the CHWTB Committee for compliance to our requirements, scientific quality, researcher institution track record and our ability to support the study through sample provision, tissue handling expertise. Once approved by the committee, CHWTB

will release the samples. CHWTB doesn't charge anything for the samples, but the researchers will need to pay for the shipments.

(4) Reuse potential

Specimen from the same patient may be used in several different projects.

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Competing Interests

The authors have no competing interests to declare.

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