The Cancer Collaborative Biobank

Key Emerging Research Infrastructure

Megan Ellis (CCB Manager)

MSH/CHR/PAH/CCB – Cancer Collaborative Biobank

TIME
IN PARTNERSHIP WITH CNN

10 Ideas changing the world right now

Biobanks

By ALICE PARK

Inside Huntsman Cancer Institute's vaults: Pancreatic tumors on ice

"Biobanks will transform the way we see disease research developing"

"..an organic bank account. You put biomaterials in and earn medical interest in the form of knowledge and treatments that grow out of that."

Thursday, Mar. 12, 2009

What is the CCB?

- The Cancer Collaborative Biobank (CCB) was created solely to help facilitate research.

- It was recognised that one of the rate limiting steps in blood cancer research was the inadequate access that researchers had to suitable biological samples & sample numbers thereby preventing their research plans.

- The biobank was designed to bridge this gap, by collecting, processing and storing samples from consented patients with a wide range of haematological diseases. By doing this, there is now a steady store of carefully categorised samples that can be requested by researchers to use in their ethically approved research projects.

- This facility is critical to increasing research into blood cancers.

Blood Cancer Samples and Research

- The Cancer Collaborative Biobank (CCB) plays a crucial role in research into leukaemia and other blood cancers by assisting our understanding of:
  - The biological processes that lead to the development of these cancers
  - Why some patients respond differently to others when given the same treatments
  - What treatment strategies will be more effective for patients with these diseases

Governance is key

- Biobanks needs to ensure they are compliant with legislative, regulatory and policy requirements of governing bodies.

- Having a local operational governance framework in place along with quality assurance procedures for the collection, processing, storage, security, retrieval and transfer of biospecimens and associated patient information is essential. This ensures compliance with requirements e.g. to protect donors identities and ensuring researcher samples are fit for purpose.

- There is no point in collecting biospecimens unless biobanks can assure researchers of the quality of all facilities processes including sample QC.

- There needs to be clear and verifiable standards of collection, annotation, storage and access

- Compatibility with international collection standards is important.

Responding to the Ethical, Legal & Social Implications of Biobanking

- **Biobanks do not operate in an ethical or regulatory void.**

- Must be in compliance with relevant legislation and regulations (Commonwealth & State)
  - » Transplantation& Anatomy Act 1979 (QLD)
  - » Information Privacy Act 2009 (QLD)
  - » Hospital & Health Boards Act 2011 (Qld)
  - » Public Health Act 2005 (Qld)
  - » Therapeutic Goods Act 1989 (Cth)
  - » Transplantation& Anatomy Regulation 2004 (QLD)

- NHMRC Statement & Guidelines
  - » Australian Code for the Responsible Conduct of Research 2007
  - » Biobanks Information Paper 2010
  - » Ethics and the Exchange and Commercialisation of Products Derived from Human Tissue: Background and Issues 2011
  - » Guidelines to Promote the Wellbeing of Animals Used for Scientific Purposes 2008
  - » National Statement on Ethical Conduct in Human Research (2007) – Updated May 2015

- International Best Practice
  - » ISBER - Best Practices for Repositories: Collection, Storage, Retrieval and Distribution of Biological Materials for Research 2012
  - » National Cancer Institute: Best Practices for Biospecimen Resources 2016

This list is not exhaustive…

Responding to the Ethical, Legal & Social Implications of Biobanking

- Metro South Health Research Biorepository Governance Framework

- MSH Research Biorepository Policy & Procedures
  - Governance, Oversight and Management
  - Strategic Oversight Committee and Compliance
  - Ethics and Participation Information and Consent Forms
  - Operational Arrangements
  - Acquisition, Attainment and Recruitment
  - Facility, Equipment, Storage and Security
  - Collection, Processing, Handling and Retrieval
  - Emergency Preparedness and WH&S
  - Material Transfer Agreements, Packaging and Shipping
  - Access and Application for Samples
  - Database Tracking, Records and Documentation
  - Quality Management System (QA & QC)

- Australian Biobanks are moving towards accreditation – certification programs are now available. The program from the Canadian Tissue Repository Network (CTRNet) is highly regarded internationally.

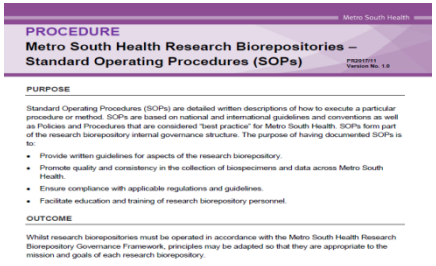
Responding to the Ethical, Legal & Social implications of biobanking

- The CCB operates under the Metro South Health Research Biorepository Governance Framework: policies, procedures, work instructions/standard operating procedures, guidelines and protocols

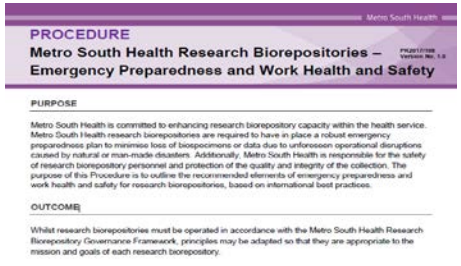
Examples:

- Research Biorepository Governance Framework documents on line within the MSH Policy index http://docs.sth.health.qld.gov.au/documents/metro-south-health


PROCEDURE
Metro South Health Research Biorepositories – Access and Applications for Samples
PURPOSE
Metro South Health is committed to promoting adherence to the highest ethical standards and practices in the release of biospecimens for research purposes. The purpose of this Procedure is to outline general principles that can be used to ensure that access to and applications for biospecimens are equitable, ethical, peer reviewed and efficient.
This Procedure applies to major ethical, legal and practical considerations that arise in the process of releasing tissue samples/biospecimens from the 'Custodian' (research biorepository) to the researchers requesting samples from the Metro South Health research biorepository.
OUTCOME
Whilst research biorepositories must be operated in accordance with the Metro South Health Research Biorepository Governance Framework, principles may be adapted so that they are appropriate to the mission and goals of each research biorepository.

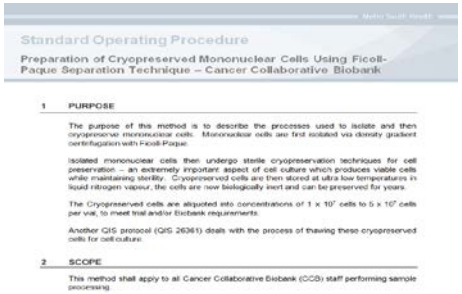

PROCEDURE
Metro South Health Research Biorepositories – Standard Operating Procedures (SOPs)
PURPOSE
Standard Operating Procedures (SOPs) are detailed written descriptions of how to execute a particular procedure or method. SOPs are based on national and international guidelines and conventions as well as Policies and Procedures that are considered "best practice" for Metro South Health. SOPs form part of the research biorepository internal governance structure. The purpose of having documented SOPs is to:
- Provide written guidelines for aspects of the research biorepository.
- Promote quality and consistency in the collection of biospecimens and data across Metro South Health.
- Ensure compliance with applicable regulations and guidelines.
- Facilitate education and training of research biorepository personnel.

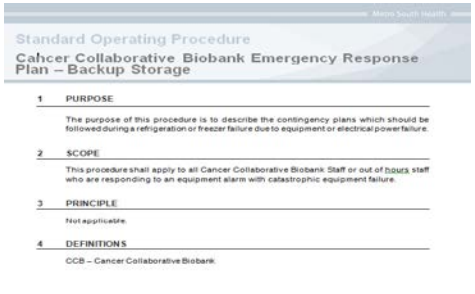
OUTCOME
Whilst research biorepositories must be operated in accordance with the Metro South Health Research Biorepository Governance Framework, principles may be adapted so that they are appropriate to the mission and goals of each research biorepository.


PROCEDURE
Metro South Health Research Biorepositories – Emergency Preparedness and Work Health and Safety
PURPOSE
Metro South Health is committed to enhancing research biorepository capacity within the health service. Metro South Health research biorepositories are required to have in place a robust emergency preparedness plan to minimise loss of biospecimens or data due to unforeseen operational disruptions caused by natural or man-made disasters. Additionally, Metro South Health is responsible for the safety of research biorepository personnel and protection of the quality and integrity of the collection. The purpose of this Procedure is to outline the recommended elements of emergency preparedness and work health and safety for research biorepositories, based on international best practices.
OUTCOME
Whilst research biorepositories must be operated in accordance with the Metro South Health Research Biorepository Governance Framework, principles may be adapted so that they are appropriate to the mission and goals of each research biorepository.

- The CCB utilises Standard Operating Procedures (SOPs) linked to criteria in the framework docs


Standard Operating Procedure
Completion of a Material Transfer Agreement (MTA)
1 PURPOSE
During the operation of a biobank, biospecimens and clinical information may be transferred to researchers at academic, university or commercial research institutions, for use in research with appropriate ethical approval. The purpose of the Material Transfer Agreement (MTA) is to ensure that before the tissue or data is shared with approved parties outside the biobank, an agreement is signed to outline the terms of the transfer, which include details regarding maintaining participant privacy, intellectual property rights (if relevant), terms for data sharing, requirements for disposal and other similar ethical and legal requirements. The purpose of this document is to outline procedures that should be followed when completing an MTA.
2 SCOPE
This Standard Operating Procedure (SOP) covers the procedures for completing an MTA once the transfer of the sample has been approved by a Research Biorepository Management Committee and Scientific Review Panel/Group which adjudicates biospecimen release. The Metro South Health MTA template must be utilised when transferring biospecimens from a Metro South Health biobank to an academic, university or commercial research institution.


Standard Operating Procedure
Preparation of Cryopreserved Mononuclear Cells Using Ficoll-Paque Separation Technique – Cancer Collaborative Biobank
1 PURPOSE
The purpose of this method is to describe the processes used to isolate and then cryopreserve mononuclear cells. Mononuclear cells are first isolated via density gradient centrifugation with Ficoll-Paque.
Isolated mononuclear cells then undergo sterile cryopreservation techniques for cell preservation – an extremely important aspect of cell culture which produces viable cells while maintaining sterility. Cryopreserved cells are then stored at ultra low temperatures in liquid nitrogen vapour, the cells are now biologically inert and can be preserved for years.
The Cryopreserved cells are aliquoted into concentrations of 1 x 10⁷ cells to 5 x 10⁷ cells per vial, to meet trial and/or Biobank requirements.
Another QIS protocol (QIS 26361) deals with the process of thawing these cryopreserved cells for cell culture.
2 SCOPE
This method shall apply to all Cancer Collaborative Biobank (CCB) staff performing sample processing.


Standard Operating Procedure
Cahcer Collaborative Biobank Emergency Response Plan – Backup Storage
1 PURPOSE
The purpose of this procedure is to describe the contingency plans which should be followed during a refrigeration or freezer failure due to equipment or electrical power failure.
2 SCOPE
This procedure shall apply to all Cancer Collaborative Biobank Staff or out of hours staff who are responding to an equipment alarm with catastrophic equipment failure.
3 PRINCIPLE
Not applicable.
4 DEFINITIONS
CCB – Cancer Collaborative Biobank

Research Regulatory Review

HREC (project-based)	Governance (site-based)
Beneficence Does the benefit of the study outweigh the risk?	Is the organisation/institution protected against any risks? Are the investigators insured? Is it the institution's risk to protect? Should there be a contract detailing who bears the risk?
Respect How will the rights of the participants be respected?	Has medical records (the data custodian) signed off?
Research merit and integrity Will the study be able to answer the questions posed?	Is there money available to complete the study? Are there resources available to complete the study? Does the study have HREC approval?
Justice Is the process of recruiting fair?	Are the recruitment processes in line with institutional policies? Has the head of the particular patient group signed and supported the project?

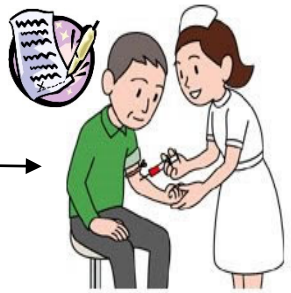
Currently CCB has two main functions:

1) **Biobanking** – processing and storage of generic tissue bank consented, trial and off-trial patients for use in future unspecified but ethically approved research.

AND

2) **Clinical Trial Service Provision** – processing and/or storage of correlative samples from patients accrued to clinical trials.

CCB Facility



TRIAL CONSENT

SPECIFIC LAB PROCESSING

DATABASE REGISTRATION

STORAGE

MTA

SAMPLE DISPATCH

PIs of CLINICAL TRIALS ONLY

Samples only for use in defined trial correlative laboratory studies

BIOBANK CONSENT

STANDARD LAB PROCESSING

DATABASE REGISTRATION

STORAGE

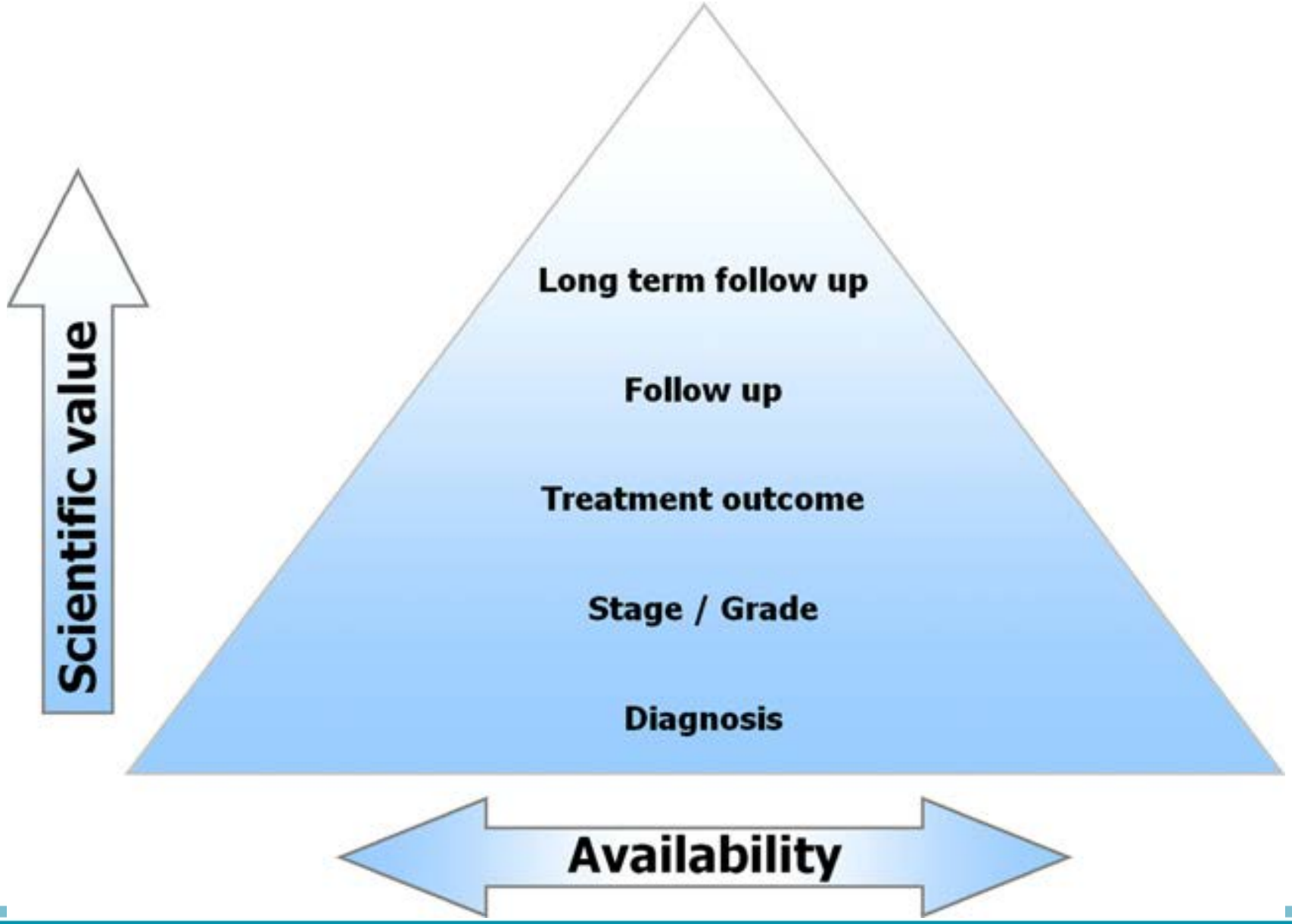
1. RESEARCHER ENQUIRY
2. DATABASE SAMPLE SEARCH and SELECTION
3. APPLICATION APPROVAL PROCESS
4. MTA
5. SAMPLE DISPATCH
6. RESEARCHER REPORTS

INDEPENDENT RESEARCHERS

Samples for use in future unspecified but ethically approved research

Translational Research

Biospecimen Value Triangle



WHO Classifications of Tumours of Haematopoietic and Lymphoid Tissues

MYELOPROLIFERATIVE NEOPLASMS

Chronic myelogenous leukaemia, *BCR-ABL1* positive	9875/3
Chronic neutrophilic leukaemia	9963/3
Polycythaemia vera	9950/3
Primary myelofibrosis	9961/3
Essential thrombocythaemia	9962/3
Chronic eosinophilic leukaemia, NOS	9964/3
Mastocytosis	
Cutaneous mastocytosis	9740/1
Systemic mastocytosis	9741/3
Mast cell leukaemia	9742/3
Mast cell sarcoma	9740/3
Extracutaneous mastocytoma	9740/1
Myeloproliferative neoplasm, unclassifiable	9975/3

MYELOID AND LYMPHOID NEOPLASMS WITH EOSINOPHILIA AND ABNORMALITIES OF *PDGFRA*, *PDGFRB* OR *FGFR1*

Myeloid and lymphoid neoplasms with *PDGFRA* rearrangement	*9965/3*
Myeloid neoplasms with *PDGFRB* rearrangement	*9966/3*
Myeloid and lymphoid neoplasms with *FGFR1* abnormalities	*9967/3*

MYELODYSPLASTIC/MYELOPROLIFERATIVE NEOPLASMS

Chronic myelomonocytic leukaemia	9945/3
Atypical chronic myeloid leukaemia, *BCR-ABL1* negative	9876/3
Juvenile myelomonocytic leukaemia	9946/3
Myelodysplastic/myeloproliferative neoplasm, unclassifiable	9975/3
Refractory anaemia with ring sideroblasts associated with marked thrombocytosis	9982/3

MYELODYSPLASTIC SYNDROMES

Refractory cytopenia with unilineage dysplasia	
Refractory anaemia	9980/3
Refractory neutropenia	*9991/3*
Refractory thrombocytopenia	*9992/3*
Refractory anaemia with ring sideroblasts	9982/3
Refractory cytopenia with multilineage dysplasia	9985/3
Refractory anaemia with excess blasts	9983/3
Myelodysplastic syndrome associated with isolated del(5q)	9986/3
Myelodysplastic syndrome, unclassifiable	9989/3
Childhood myelodysplastic syndrome	
Refractory cytopenia of childhood	9985/3

ACUTE MYELOID LEUKAEMIA (AML) AND RELATED PRECURSOR NEOPLASMS

AML with recurrent genetic abnormalities

AML with t(8;21)(q22;q22); *RUNX1-RUNX1T1*	9896/3
AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	9871/3
Acute promyelocytic leukaemia with t(15;17)(q22;q12); *PML-RARA*	9866/3
AML with t(9;11)(p22;q23); *MLLT3-MLL*	9897/3
AML with t(6;9)(p23;q34); *DEK-NUP214*	*9865/3*
AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); *RPN1-EVI1*	9869/3
AML (megakaryoblastic) with t(1;22)(p13;q13); *RBM15-MKL1*	*9911/3*
AML with mutated NPM1	9861/3
AML with mutated CEBPA	9861/3
AML with myelodysplasia-related changes	9895/3
Therapy-related myeloid neoplasms	9920/3
Acute myeloid leukaemia, NOS	9861/3
AML with minimal differentiation	9872/3
AML without maturation	9873/3
AML with maturation	9874/3
Acute myelomonocytic leukaemia	9867/3
Acute monoblastic and monocytic leukaemia	9891/3
Acute erythroid leukaemia	9840/3
Acute megakaryoblastic leukaemia	9910/3
Acute basophilic leukaemia	9870/3
Acute panmyelosis with myelofibrosis	9931/3
Myeloid sarcoma	9930/3

Myeloid proliferations related to Down syndrome

Transient abnormal myelopoiesis	*9898/1*
Myeloid leukaemia associated with Down syndrome	9898/3
Blastic plasmacytoid dendritic cell neoplasm	9727/3

ACUTE LEUKAEMIAS OF AMBIGUOUS LINEAGE

Acute undifferentiated leukaemia	9801/3
Mixed phenotype acute leukaemia with t(9;22)(q34;q11.2); *BCR-ABL1*	9806/3
Mixed phenotype acute leukaemia with t(v;11q23); *MLL* rearranged	9807/3
Mixed phenotype acute leukaemia, B/myeloid, NOS	9808/3
Mixed phenotype acute leukaemia, T/myeloid, NOS	9809/3
Natural killer (NK) cell lymphoblastic leukaemia/lymphoma	

PRECURSOR LYMPHOID NEOPLASMS

B lymphoblastic leukaemia/lymphoma

B lymphoblastic leukaemia/lymphoma, NOS	*9811/3*
B lymphoblastic leukaemia/lymphoma with recurrent genetic abnormalities	
B lymphoblastic leukaemia/lymphoma with t(9;22)(q34;q11.2); *BCR-ABL1*	*9812/3*
B lymphoblastic leukaemia/lymphoma with t(v;11q23); *MLL* rearranged	*9813/3*
B lymphoblastic leukaemia/lymphoma with t(12;21)(p13;q22); *TEL-AML1 (ETV6-RUNX1)*	*9814/3*
B lymphoblastic leukaemia/lymphoma with hyperdiploidy	*9815/3*
B lymphoblastic leukaemia/lymphoma with hypodiploidy (hypodiploid ALL)	*9816/3*
B lymphoblastic leukaemia/lymphoma with t(5;14)(q31;q32); *IL3-IGH*	*9817/3*
B lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *E2A-PBX1 (TCF3-PBX1)*	*9818/3*
T lymphoblastic leukaemia/lymphoma	*9837/3*

MATURE B-CELL NEOPLASMS

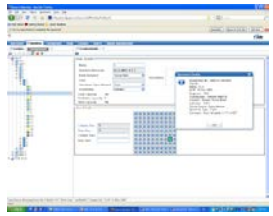
Chronic lymphocytic leukaemia/ small lymphocytic lymphoma	9823/3
B-cell prolymphocytic leukaemia	9833/3
Splenic marginal zone lymphoma	9689/3
Hairy cell leukaemia	9940/3
Splenic B-cell lymphoma/leukaemia, unclassifiable	9591/3
Splenic diffuse red pulp small B-cell lymphoma	9591/3
Hairy cell leukaemia-variant	9591/3
Lymphoplasmacytic lymphoma	9671/3
Waldenström macroglobulinemia	9761/3
Heavy chain diseases	9762/3
Alpha heavy chain disease	9762/3
Gamma heavy chain disease	9762/3
Mu heavy chain disease	9762/3
Plasma cell myeloma	9732/3
Solitary plasmacytoma of bone	9731/3
Extraosseous plasmacytoma	9734/3

Sample Processing

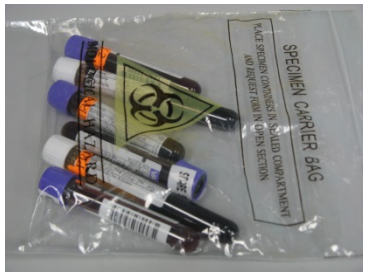
Standardization of pre-analytical handling is critically important for reliable research results

BM / PB	Product	Lab Studies
Trizol (-80°C freezer)	RNA	Gene expression
Cell Pellet (-80°C freezer)	DNA	Genomic studies
Cryopreserved cells (liquid nitrogen)	Viable cells	Cell Culture; cytogenetics; *in vitro* drug testing
Serum / Plasma (-80°C freezer)	Serum or plasma	Cytokines, Proteomics

Biospecimen life cycle



Donor TB consented & Samples collected



Sample Receipt

Sample Processing

Temp controlled storage

Researcher applies for Tissue Bank samples

Clinical Trial Correlative samples provided to PIs only

Committee Approval Process

Research

Sample Access Requirements for Researchers

1. Contact the CCB with your sample enquiry: samplecoordbiobank@health.qld.gov.au

2. A database search will be performed on current holdings. Applicable patient & sample numbers will be given.

3. Costs will be detailed. A CCB sample application & Material Transfer Agreement (MTA) will be provided

4. Part of the formal application submission requires researchers to provide:
    1. Project details and to specify sample numbers being sought
    2. HREC approval from your site for the proposed project
    3. Evidence of financial approval from your site for the project
    4. Sign off on application from Institutional Head

5. After submission, all formal applications are assessed by the CCB Research Committee

6. Before dispatch you will need:
    1. Approval from the CCB Research Committee
    2. MTA sign off between your institution and MSH
    3. To liaise with CCB staff re: sample transport (if needed)

7. After dispatch you will be:
    1. Invoiced
    2. Contacted annually for researcher reports detailing presentation & publication data (until project completion)

What are the future plans for the CCB?

- The Cancer Collaborative Biobank (CCB) wants to play a crucial role in helping to facilitate research of disease.

- In the future we hope there may be the potential to broaden disease group collections for translational research. A final decision on this will be made by MSH Executives, but to inform this, information gathering is about to begin via a research consultation survey.

- Previous surveys have informed biobanks that patients are not stoppers to research. They are keen to be involved. Their donations are altruistic - to help others in the future who one day may be diagnosed with their disease.

- The design and operation of research biorepositories is in large dictated by the intent of the collection and by cancer type, specific collection and storage requirements for the biospecimens or institution.

Researcher Consultation

- The Cancer Collaborative Biobank (CCB) wishes to invite researchers to provide input regarding sample collection, processing and storage requirements for cancer biobanking in Metro South Health.

- The following survey will be circulated widely to MSH and TRI contacts https://www.surveymonkey.com/r/Y7CQ9RZ and is available for completion online (please copy and paste the hyperlink into Mozilla Firefox to view the survey). The survey will also be circulated to contacts in the near future.

- Please note: if the survey identifies you have an interest in haematological malignancies; I would then like to contact you directly and provide an additional questionnaire which contains more targeted questions regarding requirements.

- If you have any questions in relation to this consultation please contact Megan Ellis, CCB Manager, +61 07 3176 5835 or megan.ellis@health.qld.gov.au

Acknowledgments

Cancer Collaborative Biobank Staff wish to acknowledge:

All Donors

The Centres for Health Research – Metro South Health

(in particular the Director & the Project Manager for Research Development: Paul Dall'Alba & Erica Wright)

PAH Haematologists/Registrars

Allied Health Professionals and CTU Research Nurses