Building a Bank for the Future: Developing the Maternal Research Placenta & Cord Blood Bank at Froedtert and the Medical College of Wisconsin

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ABOUT THE MCW TISSUE BANK

The Medical College of Wisconsin (MCW) Tissue Bank's mission is to capitalize and centralize collection of discard tissue, blood, and associated clinical information for intended future use in research by MCW faculty. The Bank also provides support services for MCW investigators with studies involving human specimens. The MCW Tissue Bank is dedicated to working with each investigator in order to meet research needs.

The IRB approved MCW Tissue Bank Consent Training Program has allowed the Bank to recruit in many areas of Froedtert Hospital and affiliated health partners. Some key facts about this program and its development include:

The MCW Tissue Bank collection*:

- Over 17,000 consented subjects
- We have collected and stored:
 - Blood from over 10,000 subjects
 - Tissue from over 3,350 subjects
 - Lysed bone marrow cells from over 1,270 subjects

The Maternal Research Placenta and Cord Blood Bank (MRPCB Bank) is operated within the MCW Tissue Bank. Participants consent for an individual pregnancy to donate placenta tissue, cord blood, and maternal peripheral blood to the MRPCB Bank for research purposes. These specimens are linked to the participant's clinical medical record. Participants may withdraw at any time.

MRPCB Bank includes*:

- 2,161 consented pregnancies
 - 7,939 placenta samples and 2,622 umbilical cord samples from 1265 pregnancies
 - 11,380 cord blood aliquots from 924 pregnancies
 - 1788 peripheral blood aliquots from 213 pregnancies
 - 447 specimens have been distributed to requestors
- * As of 4/19/2018

Fig 3. MCW Tissue Bank staff pictured above from lower left: Janelle Lang-Piette Research Technologist, Mary Rau Tissue Bank Manager, Mónica Thom Laboratory Assistant, Allia Nelson, Research Coordinator, Jason Kirkpatrick Research Coordinator, Mollie Patton, Pathologists' Assistant (ASCP), Ellen A. Schneider, MS, Research Technologist II, Allison Dawson Laboratory Assistant

ABSTRACT

Maternal fetal medicine is a dynamic area of research that increasingly needs high quality pregnancy related human specimens to progress. Biobanks storing placenta, cord blood, maternal peripheral blood, and associated clinical information are necessary to facilitate innovative research. However, building a bank poses challenges, especially with a vulnerable population like pregnant women. Researchers at Medical College of Wisconsin (MCW) working on the National Institutes of Health (NIH) funded Human Placenta Project (HPP) needed a functioning, hospital-integrated reproductive biobank to pursue their work and came to the MCW Tissue Bank to see what we could offer.

METHODS

There are several processes established for received samples from the MRPCB program. Maternal peripheral blood is received from campus labs and is aliquoted into one vial of whole blood + 10% DMSO, centrifuged for 15 minutes at 2600 rpm and then aliquoted further into 0.75 mL plasma samples and one buffy coat (see Fig 5 – Peripheral Blood). Post-delivery samples are received from the L&D floor. Cord blood is centrifuged for 35 minutes at 2600 rpm and then aliquoted into up to 8 plasma aliquots (previously 5 aliquots) and up to 8 buffy coats. Normal tissue samples are procured from the placenta and umbilical cord and are either snap frozen in liquid nitrogen or fixed in formalin to be processed into a FFPE block and H&E slide (see Fsizeig 6). Snap frozen tissue and blood aliquots are stored in -80 freezers.

Fig 5. Cryopreservation protocol for received cord blood and maternal peripheral blood samples.

Fig 6. Placenta and umbilical cord procurement protocol.

Fig 7. Placenta Procurement (Westra 1996)

Study	Ischemia Time	Consent Form(s) Obtained	Maximum Number of Samples per Day	Day of Week & Sample Cut off Time	Delivery Method	Current Collection Criteria
HPP1	1-2 hours from delivery ideally OR < 10 hours if refrigerated overnight	Narayan Study Consent or MRPCB Consent	Any	Monday-Friday 8 am-5 pm	Any	Singleton Only, Pre-eclamptic or control samples
HPP2	48 hours from delivery or less	Narayan Study Consent or MRPCB Consent	1	Monday-Friday 8 am-5 pm	Any	Singleton Only, Pre-eclamptic only
HPP3	1-2 hours from delivery ideally OR < 10 hours if refrigerated overnight	Narayan Study Consent or MRPCB Consent	Any	Monday-Friday 8 am-5 pm	Any	Singleton Only, Pre-eclamptic or control samples
Simple Membranes	24 hours from delivery or less	Narayan Study Consent or MRPCB Consent	1-2	Monday-Friday 8 am-2 pm	Scheduled Cesarean, no trial of labor	Singleton Only, no pathology
Complex Membranes	24 hours from delivery or less	Narayan Study Consent or MRPCB Consent	Any	Monday-Friday 8 am-5 pm	Trial of labor and then Cesarean	Singleton Only, no pathology, pre-eclamptic for pre-eclamptic but not full term
MCW Tissue Bank	Any	MRPCB Consent	Any	Monday-Friday 8 am-5 pm	Any	Any
HPP4	12 hours from delivery or less	MRPCB Consent	1-2	Thursdays only, 8 am-5 pm	Any	Singleton Only

Fig 8. Flow chart of open placenta requests for studies. The flow chart was created for simplifying fresh placenta study management for Bank staff. Investigators vet their own study criteria with a mechanism in place for requesting changes.

PROBLEMS & PROPOSED SOLUTIONS

Given the large number of interested researchers, the MCW Tissue Bank undertook the creation of the Maternal Research Placenta & Cord Blood Bank in 2014. Over the last three years, a unique consent form and consenting process was developed and implemented after close work with multiple campus teams. We have worked closely with Froedtert and MCW Labor and Delivery to optimize collection of cord blood, improved our placenta protocol through quality control, and we continually seek to revise our sample processing to aid research. Efforts to improve both maternal peripheral blood collection and processing are underway. We are also beginning to expand our program to another hospital campus within the Froedtert and MCW

Challenges	Overcoming the Challenge
Funding	Collaboration between institutional centers Continued negotiations MRPCB Workshop offered to all staff and faculty Research Coordinator outreach via emails
Expanding awareness of program to researchers	MCW – Tissue Bank Website Hospital compliance: forwards inquiring researchers to the MCW – Tissue Bank to fulfill their requests
Expanding awareness of program to consenters	Outreach/staff education Brochures Posters
Expanding awareness of program to the public	MCW – Tissue Bank Website Identifying and training consenters to begin the conversation
Maximizing access to neonate specimens	Continued bioinformatics improvements
Approvals for expansion	Identify all approvals needed for expansion to be successful with the help of hospital compliance
Identifying and training consenters	Identify management Outreach throughout the Hospital, Affiliate Hospitals and to OB providers Maintain contact with management to continue training new consenters
Consent compliance	Continued consent education Research Coordinator audits
Receiving completed consent forms from off-campus locations	Scanning completed forms and sending it either via email or fax Sending completed forms via interoffice mail
Maternal peripheral blood sample collection	Continued collaboration with Phlebotomists Continued education to OB Gyn/RMMA staff Expansion in training affiliate lab staff in the Tissue Bank order
Identifying participants on L&D	Collaboration with researchers on identifying most ideal gestational age to collect sample Collaboration with EMR team Flag in EMR
Cord blood collection	Addition of study column on the L&D EMR grease-board Identify/train L&D staff to aide providers in identifying consented participants
Cord blood collection inconsistencies	Continued OB provider education Continued education in identifying needs for clinical vs research Training material for the OB providers/residents
Placenta collection	Collaboration with MFM to identify and implement best clinical practices with OB providers Collaboration with EMR team to add a placenta order which automatically generates identification of research vs clinical needs Addition of placenta order to the admission order set
Placentas refrigerated within 2 hours from delivery	Continued education to L&D staff Implementation and use of pneumatic tubing system for timely placenta delivery to MCW Tissue Bank Collaboration with front desk team in Pathology and WI Diagnostics Laboratory Continued education in identifying needs for clinical vs research

Fig 9. Identified challenges faced when implementing the MRPCB program at the main campus, as well as affiliate, off-campus locations along with the used and proposed solutions.

CONCLUSIONS

In response to campus research need, the MCW Tissue Bank has built a dynamic collection of pregnancy related human specimens in a distinct hospital integrated biobank. With over 2100 consented participants and thousands of specimen aliquots, we have been able to support MCW researchers working on not only HPP research but other diverse research areas including immunology and cardiovascular science. Moving forward, we will continue refining protocols, working with consenters, and optimizing this program to respond to local research needs while safeguarding participant rights.

Fig 10. Number of pregnancy collection cases with expected volume

Future Direction of MRPCB

- Continued expansion of Affiliate locations
- Collaboration with Children's Hospital of Wisconsin
- Attract more Maternal Researchers to MCW
- Continued collaboration with Researchers, resulting in protocol improvements
 - Serial maternal blood samples
 - PBMC processing from maternal blood
 - Obtaining paternal blood samples
 - Change in blood cryopreservation protocols
 - Change in placenta procurement process
 - Follow best clinical practice
 - Identify best procurement timeframe from delivery

Fig 11. With the expansion to SJH, projected growth was plotted for consent based on the average number of women seen per year at the MFM clinic at SJH. The goal is to have 60% of the total number of women seen consent to the MRPCB program. Using this statistic, the L&D educator at SJH determined that the goal is to collect 100% of all placentas and 75% of all cord bloods from the consented participants. Projected growth of the program at the Froedtert location as well as anticipated SJH contribution lead to the total increase in collection of consent, placenta, and cord blood cases plotted as total increase anticipated in 2018.

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