

Development of a Pediatric Tissue Donation Program for Research that Aligns with Processes for Transplant

Patrick Van Hoose¹, Melissa Faith², Raquel G. Hernandez², Thomas G. Blanchard³, Deanne M. Taylor⁴, Rebecca L. Linn⁴, Casie Heinemann⁵, Mary Pfeiffer⁶, Ahmad Salehi⁷, Larry Suplee⁸, Rick Ryan⁸, Immanuel Rasool⁹, Michelle Gilbert¹⁰, Schawnte' Williams-Taylor¹⁰, Joseph Kreeb¹⁰, Melissa W. VonDran¹, and Thomas J. Bell¹

¹ National Disease Research Interchange, Philadelphia, PA

² Johns Hopkins All Children's Hospital, St. Petersburg, FL

³ University of Maryland School of Medicine, Baltimore, MD

⁴ Children's Hospital of Philadelphia, Philadelphia, PA

⁵ Center for Organ Recovery and Education, Pittsburgh, PA

⁶ ConnectLife, Williamsville, NY

⁷ Donor Network West, San Roman, CA

⁸ Gift of Life Donor Program, Philadelphia, PA

⁹ Infinite Legacy, Baltimore, MD

¹⁰ LifeGift, Houston, TX

Background: The Developmental Genotype Tissue Expression (dGTE_x) project is a large-scale NIH-funded initiative to address a significant gap in our understanding of how genes change throughout pediatric development. The dGTE_x project has three primary goals: 1) to create an atlas of gene expression across tissues from pediatric donors, 2) evaluate gene expression during development and 3) create a biobank of pediatric tissue and genetic data for the scientific community.

Hypothesis: Pediatric tissue donation for research can be supported at organ procurement organizations (OPOs) via recovery methods that align with transplant opportunities.

Methods: The dGTE_x Biospecimen Procurement Center (BPC) is a multi-institutional effort led by NDRI collaborating with a select number of OPOs across the US, including Center for Organ Recovery and Education (CORE), ConnectLife, Donor Network West, Gift of Life Donor Program, Infinite Legacy, and LifeGift. The project will collect biospecimens from 120 donors aged 0-18 years. OPOs utilize project-specific donor screening tools and authorization for donation to approach eligible donors and standardized recovery protocols to collect 40 tissue types from each donor to ensure suitability for scientific experimental methodologies.

Results: Here we report the screening, authorization, and recovery results of the dGTE_x project in the first year of the tissue collection effort, resulting in 25 successful donor recoveries. We provide details of procedures developed to overcome key challenges with pediatric donations for research, including coordination with medical examiners/coroners and recovery protocols that support tissue donation for allograft processing. The dGTE_x program has developed tools to coordinate screening with medical examiners/coroners, including the ability to provide pathology reports, and supporting the recovery of tissues for research post-autopsy. The heart is an organ of great interest for dGTE_x. The dGTE_x program has developed varying recovery protocols for heart to include heart apex recovery when donors are also eligible for valve donation for allograft processing.

Conclusion: The dGTE_x BPC has successfully implemented strategies for donor authorization, biospecimen collection and processing at partner OPOs for research recovery. The dGTE_x BPC remains responsive to the needs of allograft processors and medical examiner/coroners while supporting rigorous and uniform collection of human biospecimens from pediatric donors to generate consistent and reproducible experimental results to advance the field. By allowing flexibility within the recovery parameters for the project, dGTE_x can support donor families' wishes for donation for research as well as transplant. dGTE_x is an excellent example of how OPOs can support large scale, complex tissue recoveries from pediatric donors for research.

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¹National Disease Research Interchange (NDRI), Philadelphia, PA, ²Johns Hopkins All Children's Hospital, ³University of Maryland School of Medicine, ⁴Children's Hospital of Philadelphia, ⁵Center for Organ Recovery and Education, ⁶ConnectLife, ⁷Donor Network West, ⁸Gift of Life Donor Program, ⁹Infinite Legacy, ¹⁰LifeGift

Introduction



Background: The adult genotype tissue expression (GTEx) established a molecular and data analysis resource of gene expression patterns in adults; however, these patterns are relatively stable throughout adulthood. The changes in gene expression during post-natal development are largely unstudied. These changes can impact health and disease during childhood and into adulthood. The Developmental Genotype Tissue Expression (dGTEx) project is a large-scale initiative to address a significant gap in our understanding of how genes change during development.

Goals and Impact

Establishing a Groundbreaking Pediatric Biospecimen Resource

- Establish a resource database of gene expression patterns in multiple pediatric tissues
- Create a biobank of tissues and associated data for future scientific studies
- Examine family decision maker (FDMs) and tissue requester perspectives regarding pediatric donation for the advancement of scientific research

Donor Eligibility

Age

- 0-18 years old

Infectious Disease Risk Exclusion Criteria

- History of and/or exposure to HIV/AIDS, HCV, or HBV
- History of IV drug use in the last 5 years

Hospital Admission Details Exclusion Criteria

- Whole blood transfusion in last 48 hrs
- Current positive blood cultures (sepsis)
- Hospitalization or death due to COVID

Past Medical History Exclusion Criteria

- Current or Metastatic cancer
- Chemo-radiation in the past 24 months
- Known chromosomal or genetic disorder
- Failure to thrive or total parenteral nutrition

Brain Only Exclusion Criteria

- Death caused by brain injury or head trauma
- Ventilator time > 24 hrs

- **Recovery must be able to begin within 24h of cross-clamp or cardiac cessation**
- **OPOs utilize dGTEx specific donor screening tools to identify eligible donors**

Tissue Collection

- | | |
|--------------------------------|---------------------------------------|
| • Whole Blood* | • Whole brain |
| • Stomach and digestive tract* | • Whole heart with associated vessels |
| • Muscles* | • Whole lung with airways |
| • Neurological tissues | • Pancreas |
| • Adipose* | • Reproductive tissue |
| • Skin* | • Spleen and lymph nodes* |
| • Liver | • Aorta* |
| • Kidney | • Endocrine glands |

* Minimum List of Tissues (20 tissues)

Frozen → Biobank

Fixed → Pathology

Fresh → Isolation of fibroblasts (skin) and leukocytes (blood)

Tissue Sampling Designs for Pediatric Donor Challenges

- Not all tissues are required for dGTEx allowing flexibility for alignment with transplant opportunities and medical examiner/coroner needs
- Tissue samples size is small (2.5cm x 1cm x 1cm) for most tissues
- Pathology reports for whole organs (brain, lung and heart) can be provided upon request
- Medical examiner/coroner infographic and education materials provided to OPOs
- Varying recovery protocols for heart

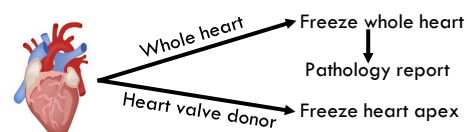


Figure 1. Differing heart recovery protocols align with tissue processor and/or medical examiner/coroner needs

Program Year 1 (PY1) Donations

PY1 Donors Screened, Authorized and Recovered

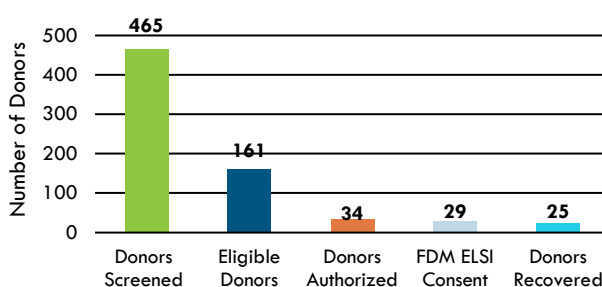


Figure 2. PY1 Donor Authorization and Recovery. Twenty-five donor recoveries have occurred with 21% of FDMs of eligible donors authorizing tissue donation with 18% FDMs consenting for ELSI study.

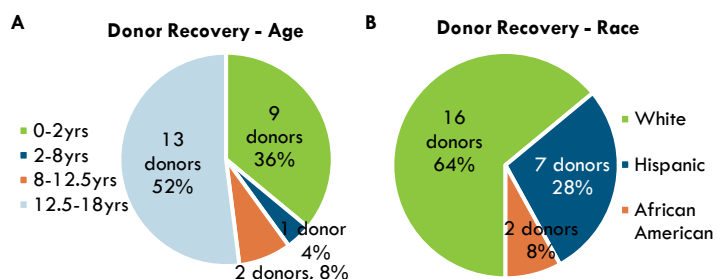


Figure 3. PY1 Donor Recovery by Age and Race. Donor recoveries by age (A) and race (B) indicate diverse donor race and age distribution concentrated in the 0-2yrs and 12.5yrs age categories. Most donor recoveries have been male (20 donors) with 5 female donors.

Conclusions

- The dGTEx BPC has successfully implemented strategies for donor authorization, biospecimen collection and processing with multiple OPO partners for pediatric donors that align with transplant processes
- The dGTEx program aligns with needs of allograft processors and medical examiner/coroners while supporting families wishes for donation to research
- Contact NDRI to learn more about dGTEx or if interested in participating (pvanhose@ndriresource.org). The current dGTEx OPO network includes: ConnectLife, Center for Organ Recovery and Education, Donor Network West, Gift of Life Donor Program, Infinite Legacy and LifeGift.
- The dGTEx BPC will be screening for pediatric donations for ~35 months