Concept Clearance: Developmental Genotype-Tissue Expression (dGTEx)

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Outline

- GTEx accomplishments
- dGTEx
  - Background
  - Proposal
  - Preparatory work
  - Consortium model
  - Budget
GTEx Accomplishments

- Established rapid autopsy program
- 965 donors (2010-2016)
- Surveyed gene expression in 53 tissues
- Provided new approach to map gene expression
- Decoded regulatory regions of genome

Over 2,000 consortium and non-consortium papers and 2\textsuperscript{nd} most data access requests
Recommendation:
Creation of a genotype-tissue expression project for neonates and children.
Why Developmental?

A child is not a small adult.

(World Health Organization, July 2008)
Differences in Development

- Metabolism
- Endocrine function
- Immune function
- Drug response
- Exposure and susceptibility to environmental toxins
Goal: Establish resource database to study gene expression patterns across developmental stages.

- Fill key gaps in understanding gene expression in human development
- Provide insight on functional networks and pathways
- Understand how gene expression affects clinical factors (ex. drug response)
Proposal: Developmental Genotype Tissue Expression (dGTEx)
Objectives

Create an **atlas of tissue gene expression** on bulk tissues and single cell populations.

Analyze **regulatory variation** and its effect on gene expression.

Create and make available **biobank of tissues and associated data** for further characterization.
Study Design

- Early post natal (0-2 yrs)
- Pre-pubertal (8-12.5 yrs)
- Post-pubertal (12.5-18 yrs)

- Sequencing (WGS, RNA)
- Biospecimen collection (blood, bulk tissue and single cell)

- Chromatin accessibility
- Histone modification
- DNA methylation
Bioethics Preparatory Work

Explore ethical issues of posthumous genomic research in neonatal and pediatric settings

- Engage community
- Eligibility criteria
- Consent
- Follow up
Families amenable towards organ donation research

Work with existing infrastructure (Organ Procurement Organizations)
Consortium Organization

Tissue Procurement Center(s)
- Recruitment
- Pathology review
- Clinical data collection
- ELSI research

Tissue aliquots

LDACC
- Laboratory
- Data Analysis
- Coordinating Center

Statistical Analysis Data Integration

NIHCHD

NHGRI
LDACC Organization

**Laboratory**
- Purify nucleic acids (DNA and RNA)
- Perform whole genome and RNA sequencing
- Maintain biobanking facility

**Data Analysis**
- Perform basic genotyping and expression analyses
- Single cell analysis
- Deposit datasets in data repositories

**Coordinating Center**
- Work with Tissue Procurement Centers
- Monitor study progress and laboratory performance
- Prepare statistical and other reports
# Distribution of Funds
*(Dollars in Thousands)*

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<th>Solicitations</th>
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**NICHD Council Approved**

Not yet developed

| TOTAL*              | 5,900  | 6,400  | 6,400  | 5,000  | 4,800  | 28,500 |

*Total cost will be split between NHGRI and NICHD. Other ICs approached for additional funding.*
Potential NIH Collaborations

Deeper Resource

~$6M/yr TC
120 donors
Limited donors and analyses

$10M/yr TC
200 donors
Increase statistical power
Establish role(s) of genes and regulatory elements

Addresses key strategic needs

Fills gap in genomic data resources
Ongoing Activities

• Human BioMolecular Atlas Program (HuBMAP) – develop open and global platform to map healthy cells in the human body primarily in adults
• Pediatric Cell Atlas (PCA) – understanding molecular characteristics of normal cells from children’s tissues

\[ \text{dGTEx} \text{ – augment and complement single cell analysis from different developmental time points} \]
# Project Timeline

**Year 1**
- Protocol development
- Network organization

**Years 2-4**
- Sequencing and tissue procurement ramp up
- Data analysis

**Year 5**
- Ramp down
- Continue analysis