

Concept Clearance: Developmental Genotype-Tissue Expression (dGTEx)

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National Human Genome
Research Institute



Eunice Kennedy Shriver National Institute
of Child Health and Human Development

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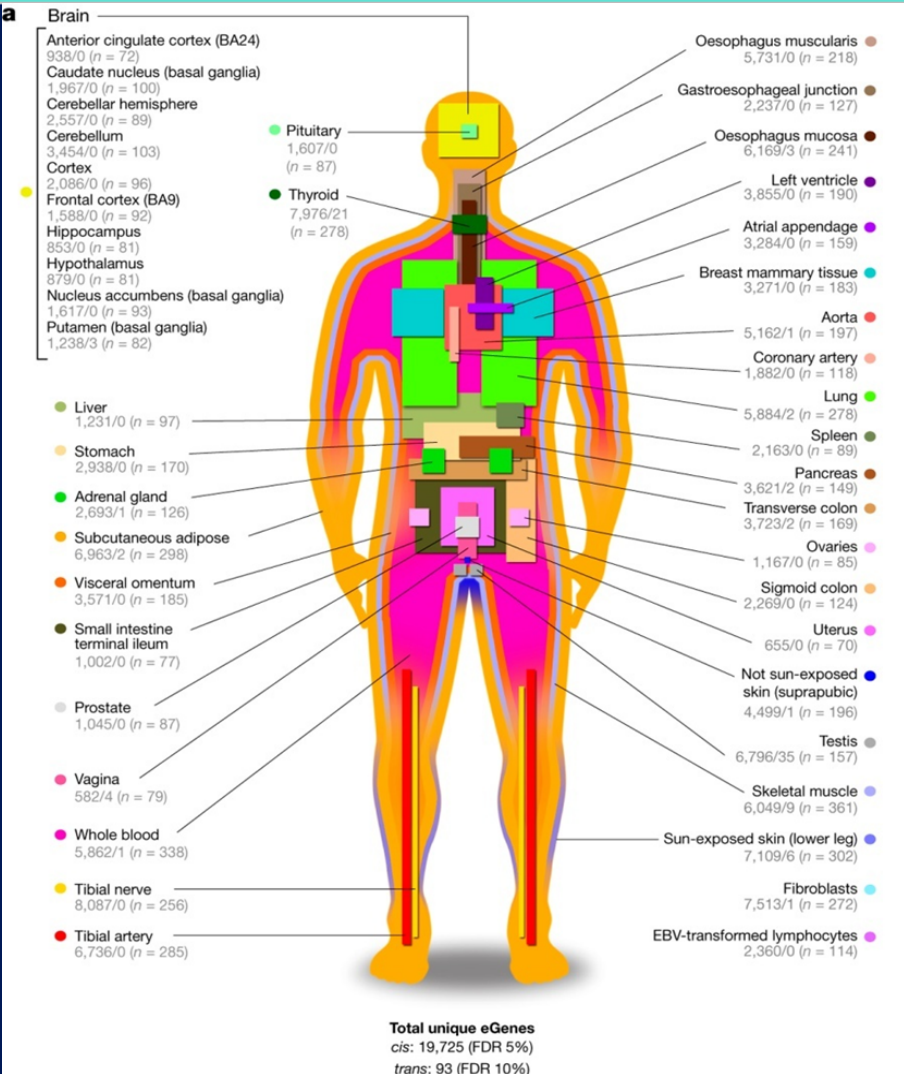
Outline

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- GTEEx accomplishments
- dGTEEx
 - Background
 - Proposal
 - Preparatory work
 - Consortium model
 - Budget



GTEx Accomplishments



Genetic effects on gene expression across human tissues

- 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 2nd most data access requests

Genomic Medicine for Reproductive, Prenatal, and Neonatal Health Workshop

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Recommendation:
Creation of a genotype-tissue expression project for neonates and children.



Scientific Community

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AGBT 2019

Strategic
Planning
meetings



ASHG 2019

World Congress
Psychiatric
Genetics

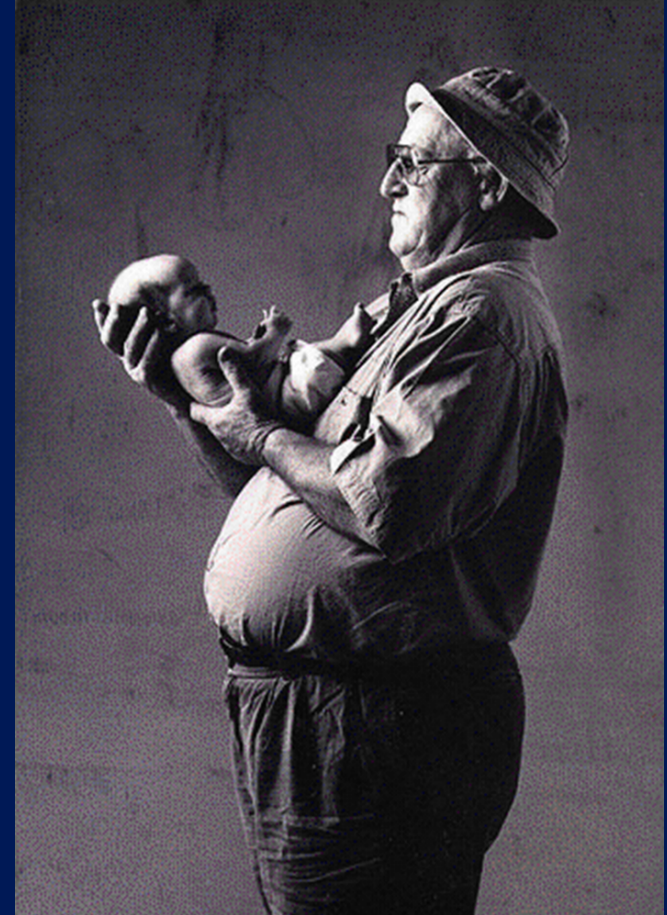
*What about expression in
developing human?*

Why Developmental?

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A child is not a small adult.

(World Health Organization, July 2008)



Differences in Development

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- 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.

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- 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)

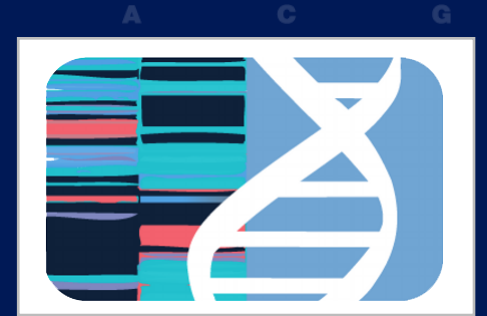


Proposal: Developmental Genotype Tissue Expression (dGTEx)

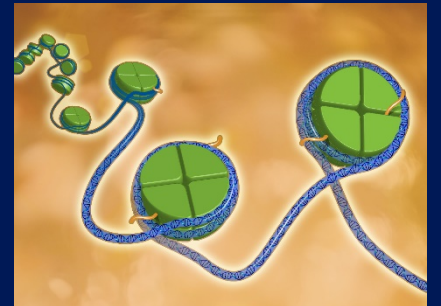


Objectives

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



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

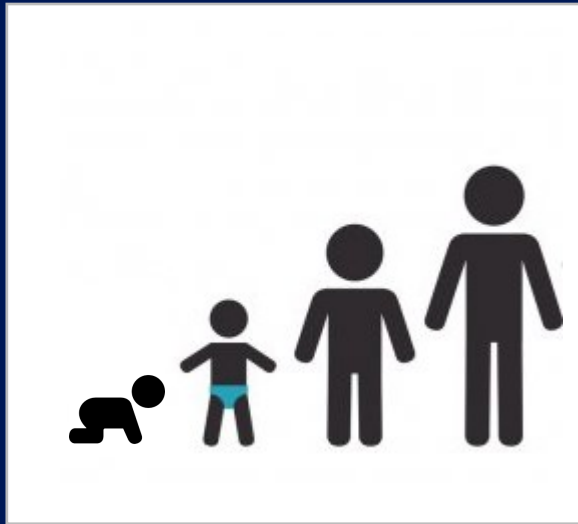


Create and make available **biobank of tissues** and **associated data** for further characterization.



Study Design

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- 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

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

- Engage community
- Eligibility criteria
- Consent
- Follow up



Tissue Procurement Feasibility



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

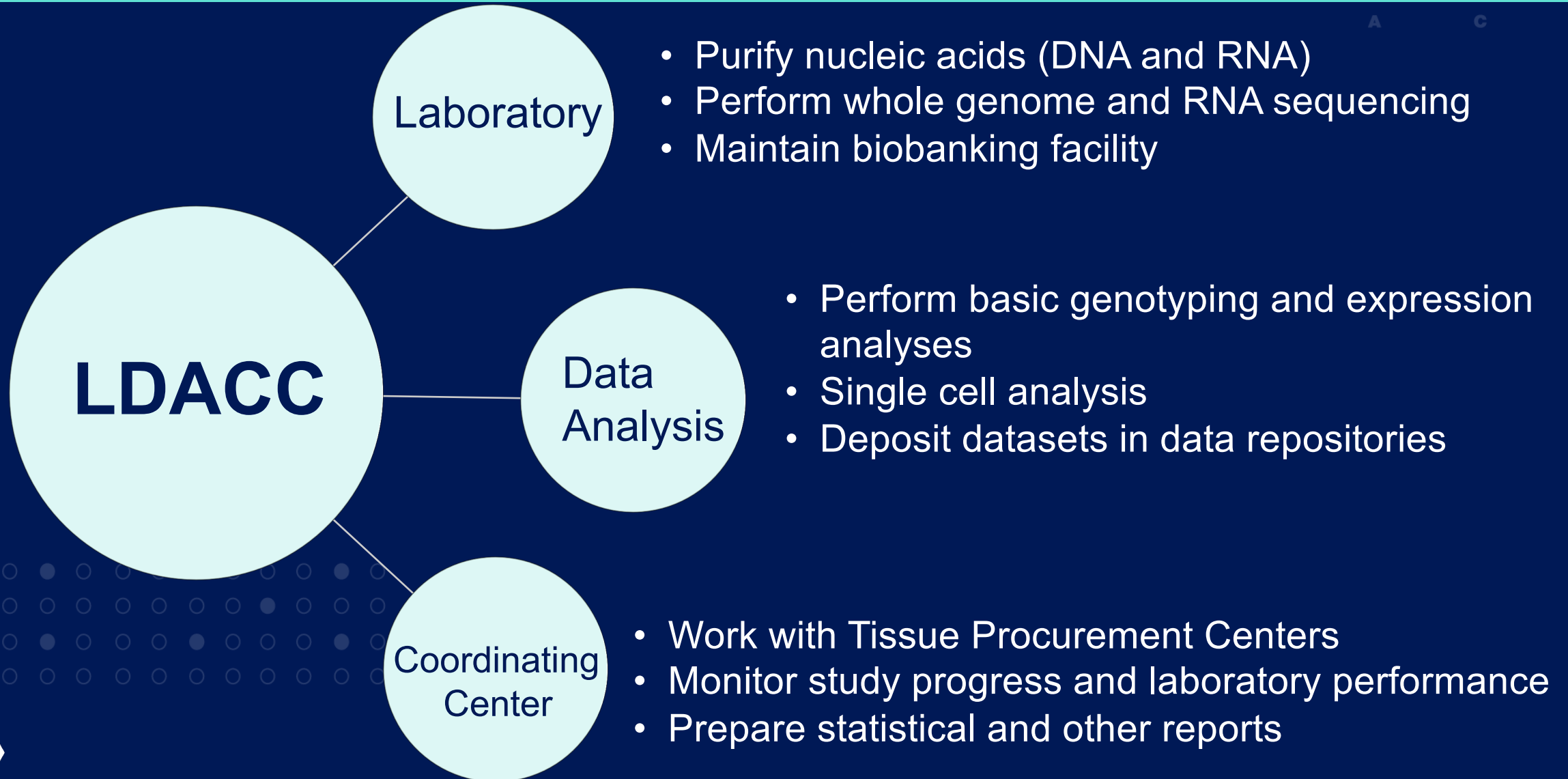
Tissue aliquots

LDACC

- Laboratory
- Data Analysis
- Coordinating Center

Statistical Analysis
Data Integration

LDACC Organization



Distribution of Funds

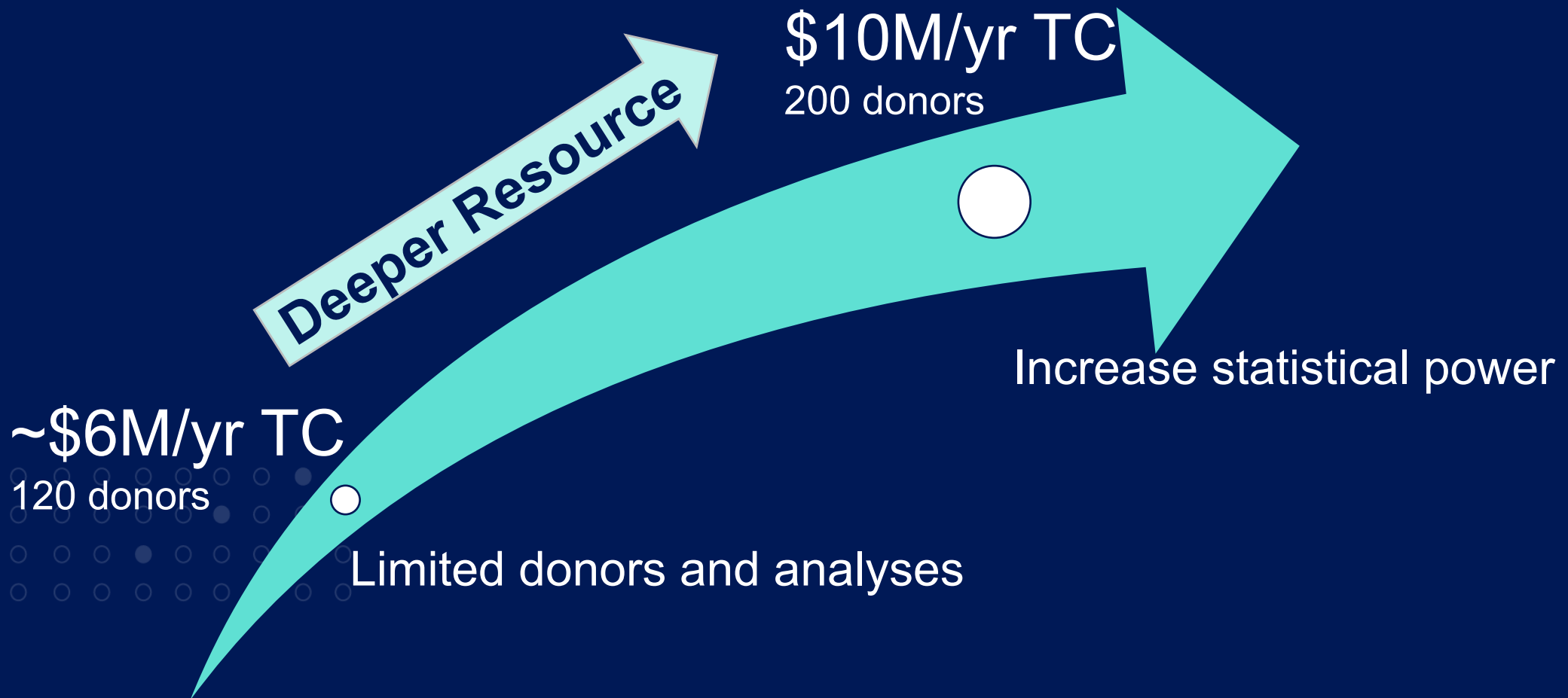
(Dollars in Thousands)

Solicitations	FY2021	FY2022	FY2023	FY2024	FY2025	TOTAL
LDACC	2,400	4,200	3,100	2,600	2,400	14,700
NICHD Council Approved						
Not yet developed						
TOTAL*	5,900	6,400	6,400	5,000	4,800	28,500

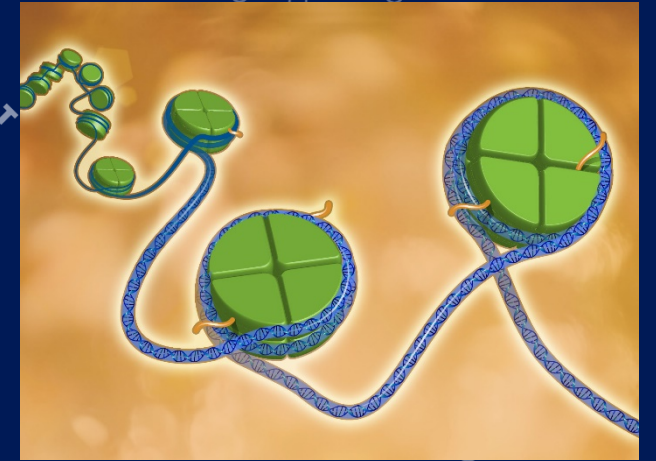
*Total cost will be split between NHGRI and NICHD. Other ICs approached for additional funding.

Potential NIH Collaborations

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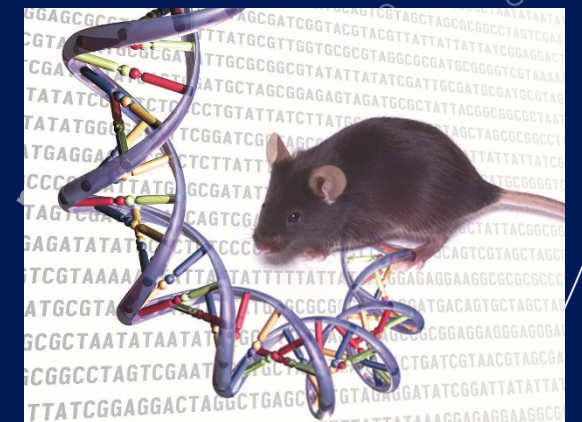


Establish role(s) of genes and regulatory elements



Addresses key strategic needs

Fills gap in genomic data resources



Council Discussion



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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



dGTE_x – augment and complement single cell analysis from different developmental time points

Project Timeline

