Non-Human Primate Developmental Genotype-Tissue Expression (NHP dGTEx)

Jennifer Troyer for the dGTEx Working Group

NHGRI: Jyoti Dayal, Joy Boyer, Laurie Findley, Simona Volpi

NICHD: Tuba Fehr, John Ilekis, Danuta Krotoski, Melissa Parisi

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

NIH National Human Genome Research Institute

The **Forefront** of **Genomics**

Purpose of NHP dGTEx

Study gene expression patterns in multiple reference tissues across developmental stages in NHPs and compare them to human gene expression patterns

- Determine common developmental networks and pathways
- Identify developmental patterns that are primate- or human-specific
- Establish datasets and samples for comparative developmental genomics
- Inform model selection for functional and developmental studies

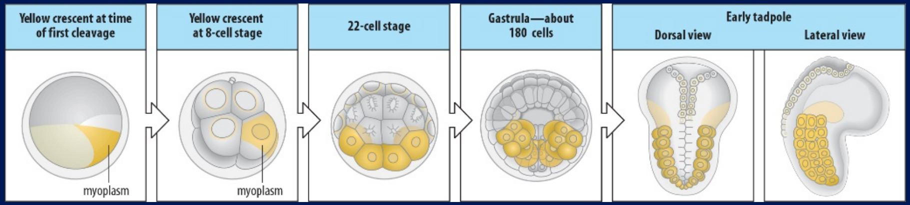
NHGRI

Genotype-Tissue Expression Projects

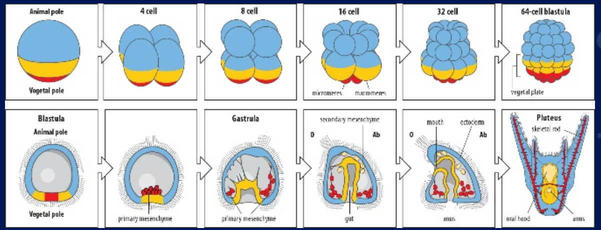
- GTEx – Common Fund program (complete)
  - 838 postmortem adults, 49 tissues; DNA and RNA seq
  - Tissue-specific gene expression profiles, eQTLs, highly used resource
- dGTEx – NHGRI, NICHD, NIMH, NINDS (beginning)
  - 120 postmortem infants and children, 30+ tissues; DNA and bulk and scRNA seq
  - Developmentally regulated tissue-specific expression
  - Impact of variation on development
- dGTEx NHP – NHGRI (proposed)
  - Experimentally tractable laboratory animals
  - Enable comparative developmental genomics
  - Build on developmental knowledge from model and other organisms

NIH NHGRI

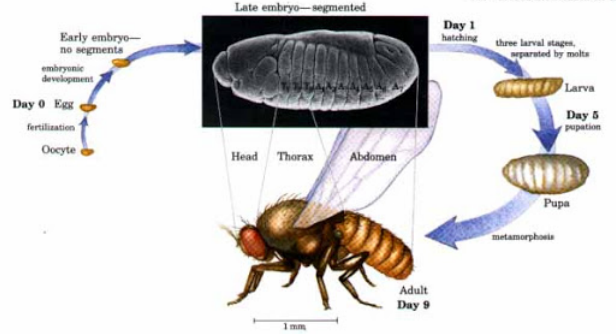
Developmental genomics in model systems



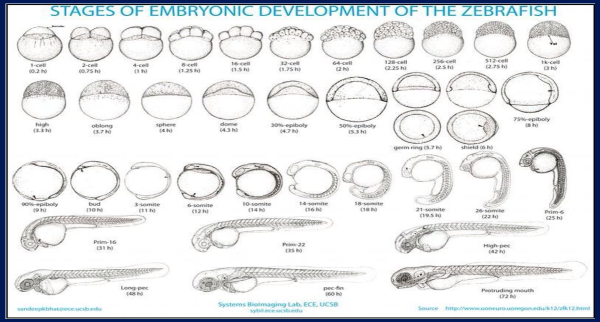
WORM



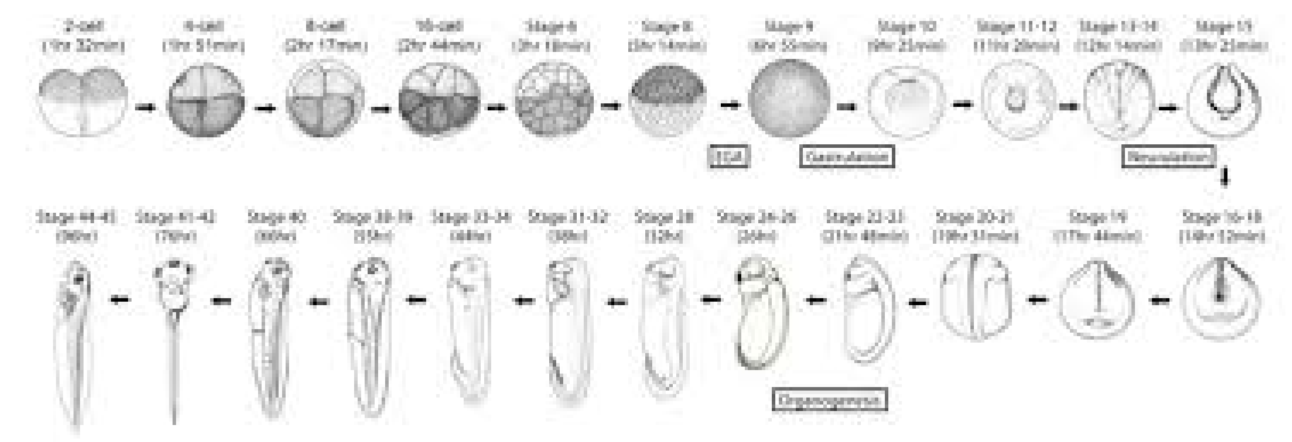
SEA URCHIN



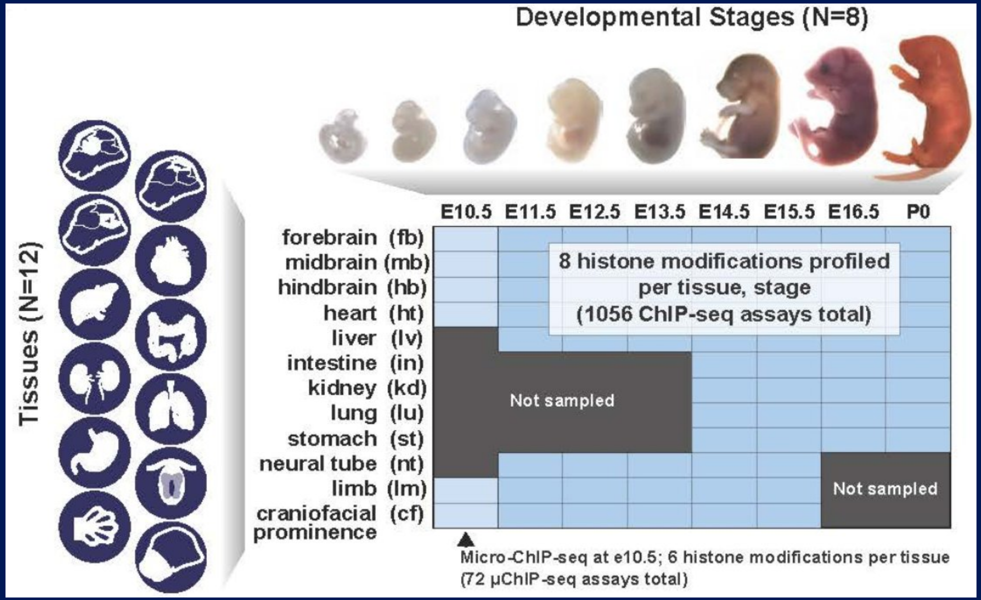
FRUIT FLY



ZEBRAFISH



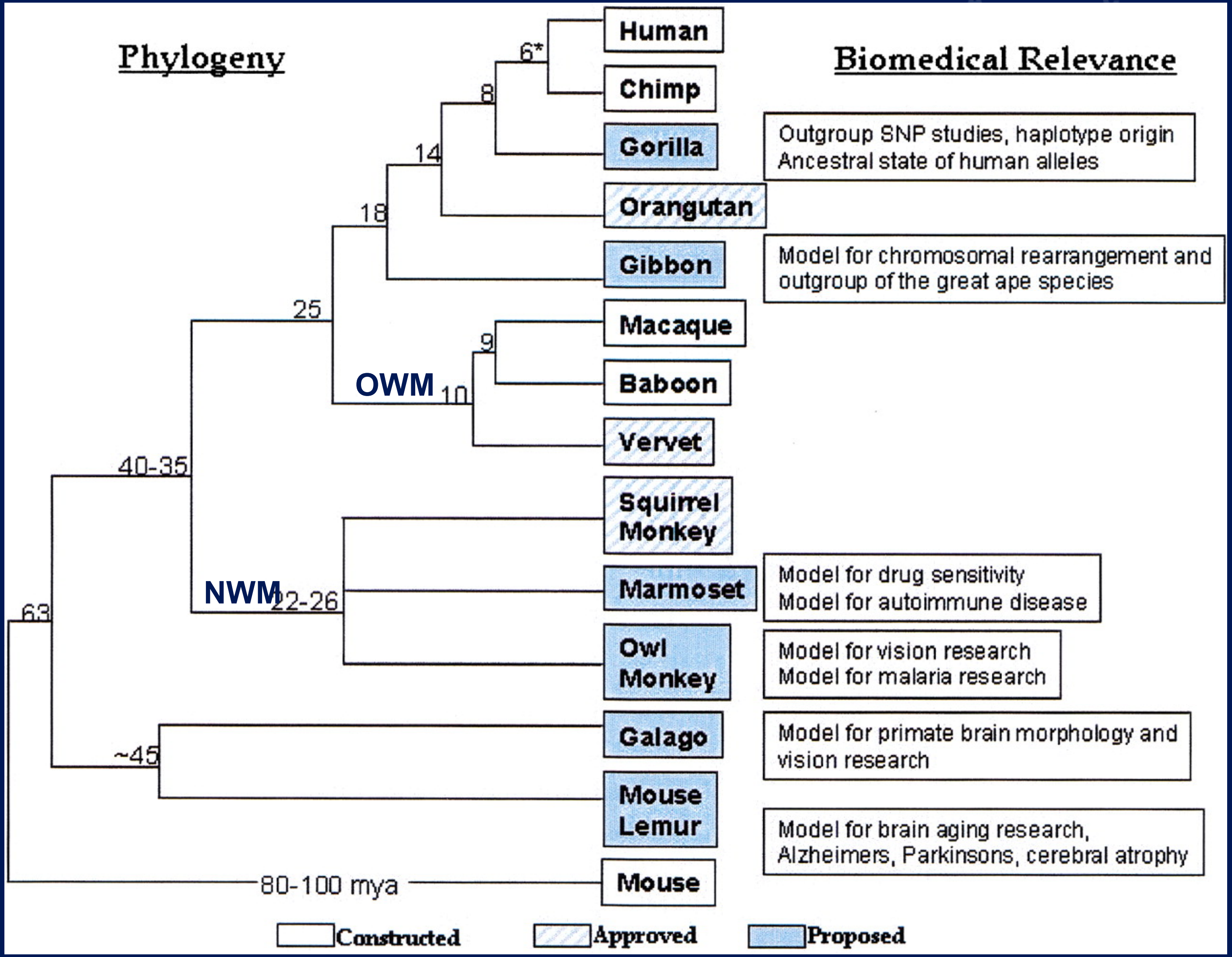
FROG



MOUSE

NHP advantages

- Close relatives
- Similar development
- Genomic diversity
- Biomedical models
- Comparative genomics



Biomedical Applications and Studies of Molecular Evolution: A Proposal for a Primate Genomic Library Resource. Evan E. Eichler and Pieter J. DeJong

NHP dGTEx Proposal

1-2 NHP Centers

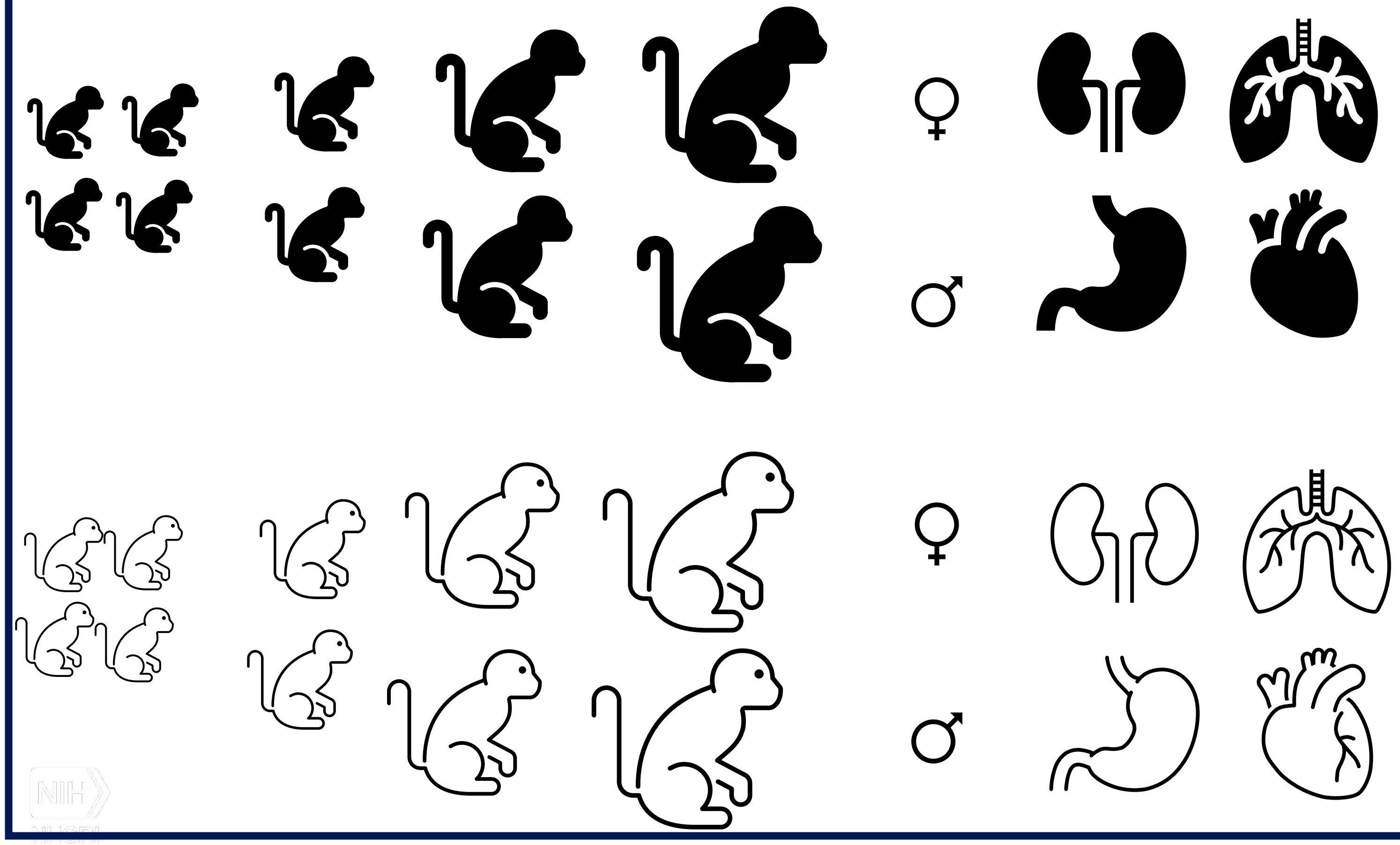
$17.5M Over 5 years ($3.5M/year)

- Expression data
  - Multiple developmental stages, tissues, species
  - May propose additional assays – single cell encouraged
- Make data available and useable to the community
- Use opportunistic and banked samples where possible

NHP dGTEx Centers

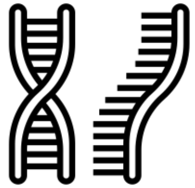
Provide Samples:

2 species (Old World and New World) X 6 stages (prenatal and postnatal) X 12 animals (male and female) X 30 tissues

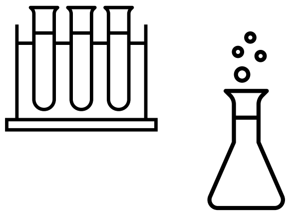


Generate Data:

WGS for each animal, RNAseq for each tissue

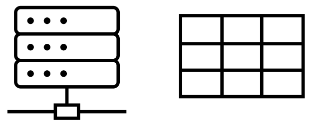


Other assays TBD

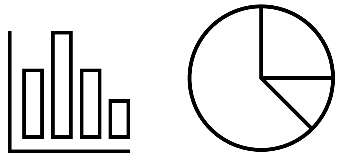


Manage Data:

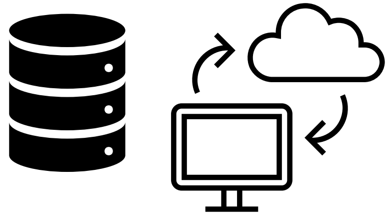
QC



Basic analyses



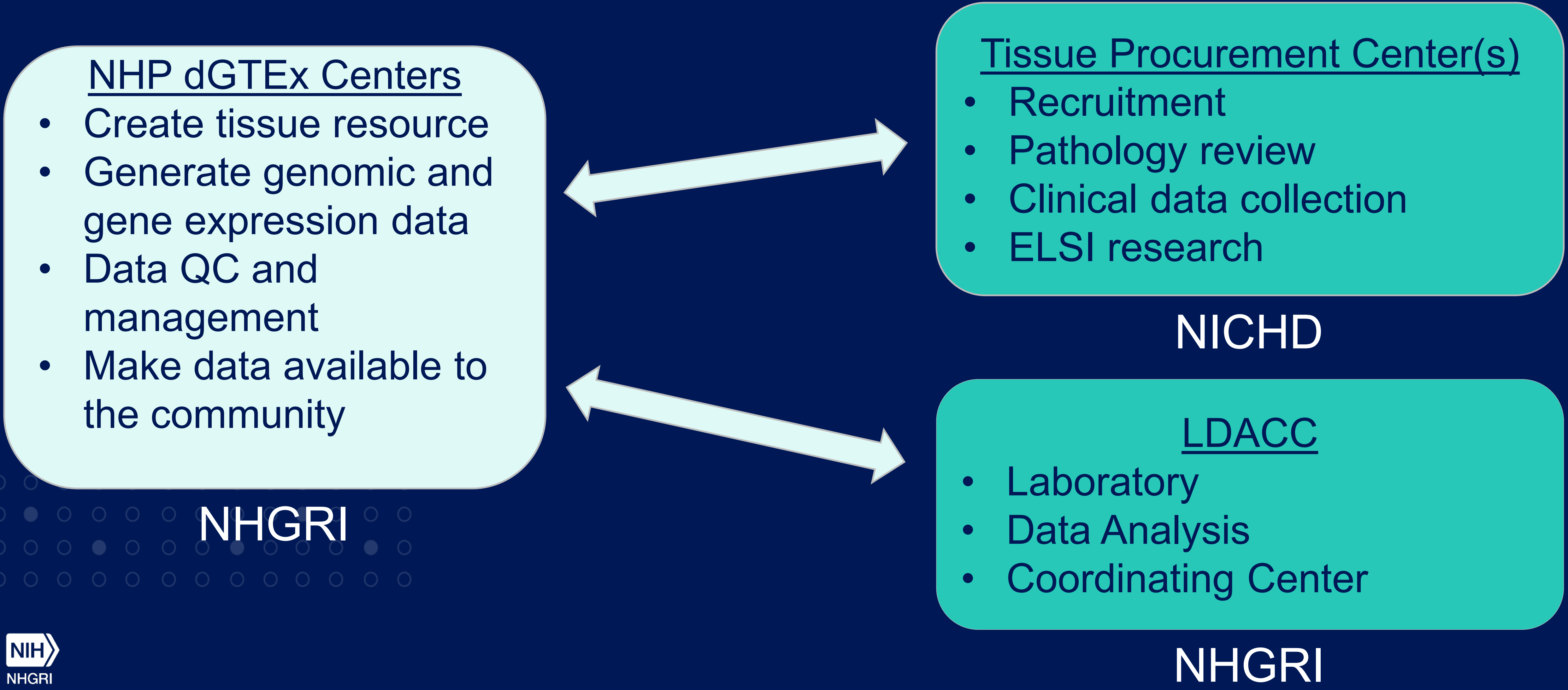
Submission to appropriate resources



Leverage NHP Resources

- National Primate Resource Center Consortium
  - 7 Centers supported by ORIP
  - Colonies from 10 species
    - Genomic resources/genetic diversity
  - High ethical standards for primate research
  - Behavior and phenotypic data
- Banked tissue samples
- NHP high quality reference genomes

Ensure Interoperability with dGTEx



NHP dGTEx Centers

- Create tissue resource
- Generate genomic and gene expression data
- Data QC and management
- Make data available to the community

NHGRI

Tissue Procurement Center(s)

- Recruitment
- Pathology review
- Clinical data collection
- ELSI research

NICHD

LDACC

- Laboratory
- Data Analysis
- Coordinating Center

NHGRI

Considerations of balance

- Multidimensional data
  - Developmental stages, individuals, tissues, assays, species
- Data integration
  - New vs. existing resources
  - New data analysis methods

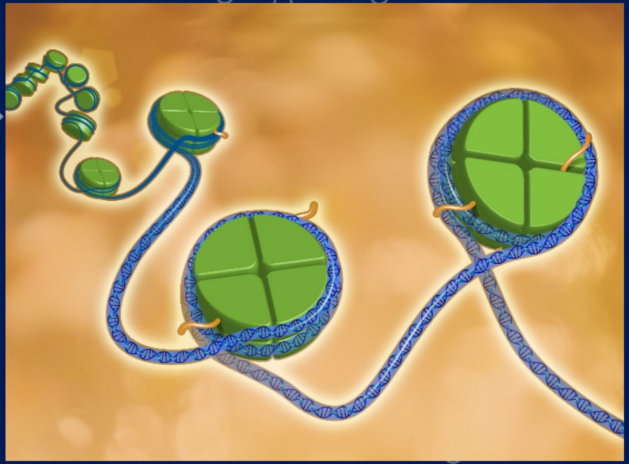
Questions

- Is the balance right? How do we maximize the benefit of these samples?
- Are there additional resources /opportunities for collaboration that we should be considering?

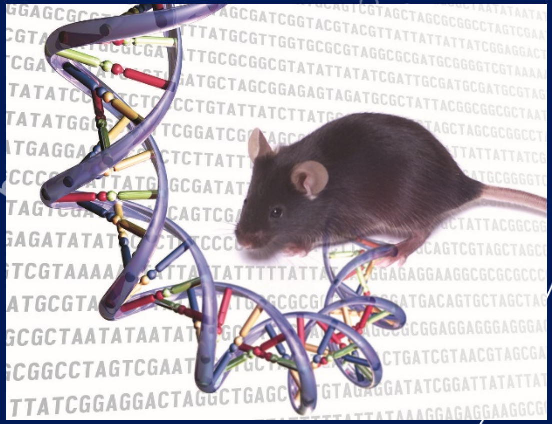
The **Forefront**
of **Genomics**®

Genome structure and function

Use evolutionary and comparative genomic data to maximize the understanding of genome function



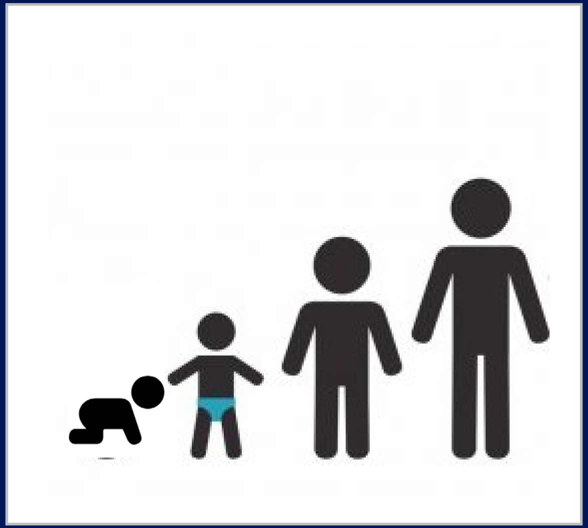
Addresses key strategic needs



Comparative genomics

- Reduce noise and increase power in human studies
- Filter for both conserved and specialized function
- Correlate genomic differences with specific traits and phenotypes
- Identify similarities across species in order to select appropriate laboratory models for specific human developmental processes and stages

Background-dGTEx Study Design



- Early post natal (0-2 yrs)
- Childhood (2-8 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

Relationship to other projects

- GTEx and dGTEx
- MODS and AGR
- KO studies (KOMP, gnomAD)
- Clinical studies/resources that seek to interpret variants and their impact on development (ClinGen, UDN)
- NHP genomic resources