

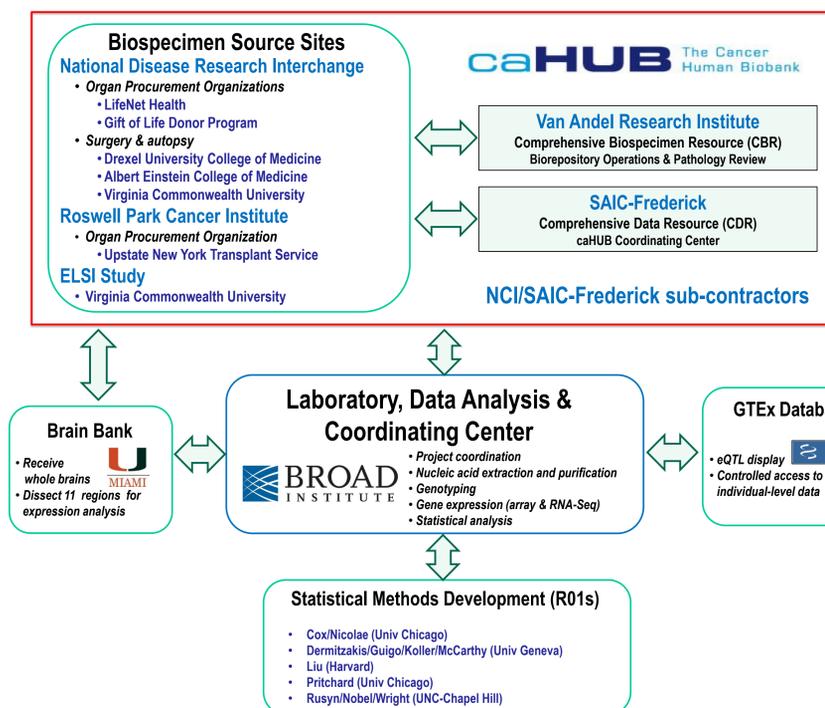
The Genotype-Tissue Expression (GTEx) Project

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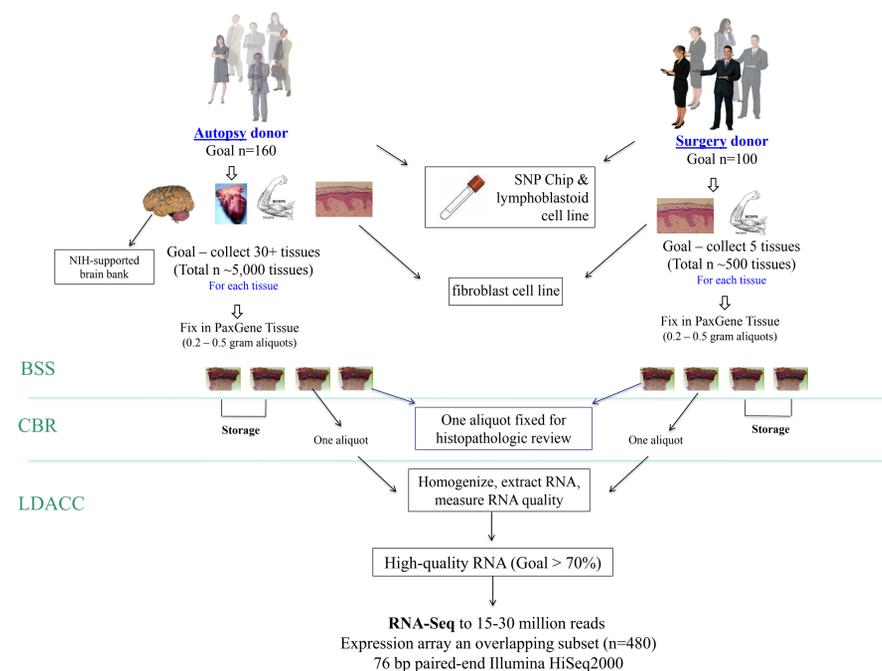
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GTEx Project Infrastructure Overview



GTEx Sample Collection and Processing



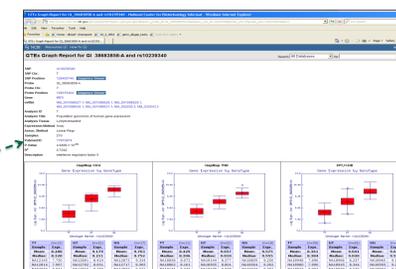
Current Tissues Collected

- Blood (Paxgene Tube)
- Fibroblast Cell Line
- Lymphoblastoid Cell Line
- Pituitary
- Prostate
- Skin
- Spleen
- Stomach
- Testis
- Thyroid
- Uterus
- Vagina
- Brain – Cerebellum
- Brain – Frontal Cortex
- Overnight shipped Brain Regions
- Brain – Cerebellum
- Brain – Frontal Cortex (BA9)
- Hippocampus
- Substantia nigra
- Anterior cingulate cortex (BA24)
- Amygdala
- Caudate (basal ganglia)
- Nucleus accumbens (basal ganglia)
- Putamen (basal ganglia)
- Hypothalamus
- Spinal cord (cervical c-1)
- Adipose
- Adrenal Gland
- Artery – Aorta
- Artery – Coronary
- Artery – Tibial
- Bladder
- Breast - Mammary Tissue
- Cervix – Ecto & Endocervix
- Colon
- Esophagus – Mucosa & Muscularis
- Fallopian Tube
- Heart
- Kidney – Cortex & Medulla
- Liver
- Lung
- Muscle – Skeletal
- Nerve – Tibial
- Ovary
- Pancreas

Highlighted brain tissues are used to compare immediate PaxGene & Frozen

GTEx Websites

- GTEx Common Fund Website: <http://commonfund.nih.gov/GTEx/>
- Resource for GTEx Donors and Families: <http://www.genome.gov/gtex>
- GTEx Database (eQTL Browser screenshot below): <http://www.ncbi.nlm.nih.gov/gtex/>



GTEx Pilot Milestones – Current Status

- Enrollment of ~10 post-mortem donors/month**
 - May 2011 – February 4, 2012: 100 donors total
 - Overall average of ~11 donors/month
- RNA samples with RNA Integrity Number (RIN) ≥ 6 for at least 70% of 12 tissues**
 - Based on analysis for the first 57 donors (average of 26 tissues collected):
 - 62% (909/1457) samples have RIN>6
 - Over 70% of 12 tissues have RIN>6
 - Biospecimens collected as of January 31, 2012:
 - 2300 Paxgene Tissue Aliquots
 - 440 Frozen Brain Tissue Samples (Brain Bank)
- Identify cis-eQTLs for 4-10% of transcripts**
 - Samples size thus far is too small to calculate cis-eQTLs. However, genotyping and expression profiling are underway. The expected analysis by March 2012 includes:
 - Genotyping (5M Illumina): 48 donors
 - Expression Arrays (Affymetrix GeneArray Expression): 480 samples
 - Transcriptome Sequencing/RNA-Seq (Illumina HiSeq2000): 290 tissues

Recent News

- Principal investigators and project officers in the GTEx consortium convene bi-annually in the Washington D.C. area to discuss operational progress and data analyses efforts. Meeting agendas, summaries and participant lists are posted on the **Common Fund website**.
- A **brochure and website for GTEx Donors and Families** were developed and now supplement the consent process.
- A **public data release** is scheduled for **Summer 2012**.
- Efforts to support a **scale-up GTEx project** are underway. The GTEx External Scientific Panel (see table) provides input to the GTEx project and will assess the criteria to scale up GTEx beyond the pilot project.

GTEx ESP Member	Institution
David L. Rimm, M.D., Ph.D.	Yale University School of Medicine, New Haven, CT
Kevin K. Brown, M.D.	National Jewish Health, Denver, CO
Vivian G. Cheung, M.D.	University of Pennsylvania School of Medicine, Philadelphia, PA
Ross Hardison, Ph.D.	Pennsylvania State University, University Park, PA
Allan Jones, Ph.D.	Allen Institute for Brain Science, Seattle, WA
Rebecca Pentz, Ph.D.	Emory University School of Medicine, Atlanta, GA

Benefits of GTEx

In summary, GTEx will provide the research community with the following:

- A public resource of comprehensive RNA expression levels in multiple tissues from densely genotyped donors
- Data to follow up on GWAS and evaluate whether a disease-associated variant is correlated with expression in a relevant tissue
- Powerful approach to identifying control sequences and networks
- Biospecimen archive for future downstream studies of regulatory non-coding RNAs, chromatin modifications, proteomics, etc.

Understanding the role of variation in the human genome is crucial to elucidating genetic contributions to human health and disease. Despite the results of genome-wide association studies (GWAS) documenting strong statistical associations between genetic variation and human traits, the functional role for most of these variants is largely unexplained. Nearly 90% of these GWAS-implicated sites lie outside of protein-coding sequences, suggesting that these variants might regulate gene expression.

The Genotype-Tissue Expression (GTEx) project was launched in 2010 as a 2.5-year project sponsored by the NIH Common Fund with the goal of assessing the feasibility of collecting high-quality RNA from multiple tissues from healthy donors. The project will collect and analyze RNA levels in 30+ human tissues from 160 postmortem donors and 4-6 tissues from 100 surgical controls that have been characterized for germline genetic variation through dense genotyping. The resulting data will be made available to the scientific community through an NIH-supported GTEx database.

By treating RNA expression levels as quantitative traits, expression quantitative trait loci (eQTLs) will be identified as sites containing genetic variation that correlate with changes in RNA expression. Such eQTLs have been associated with 4%-12% of expressed human genes, and with common complex human diseases, including obesity, atherosclerosis, type 2 diabetes, Crohn's disease, and asthma. Additionally, only few studies have examined the tissue specificity of eQTLs. The GTEx project will thus serve as a resource database and tissue bank for many future studies, especially for understanding the functional basis of inherited susceptibility to disease.

