

Overview of GTEx Biospecimen Collections

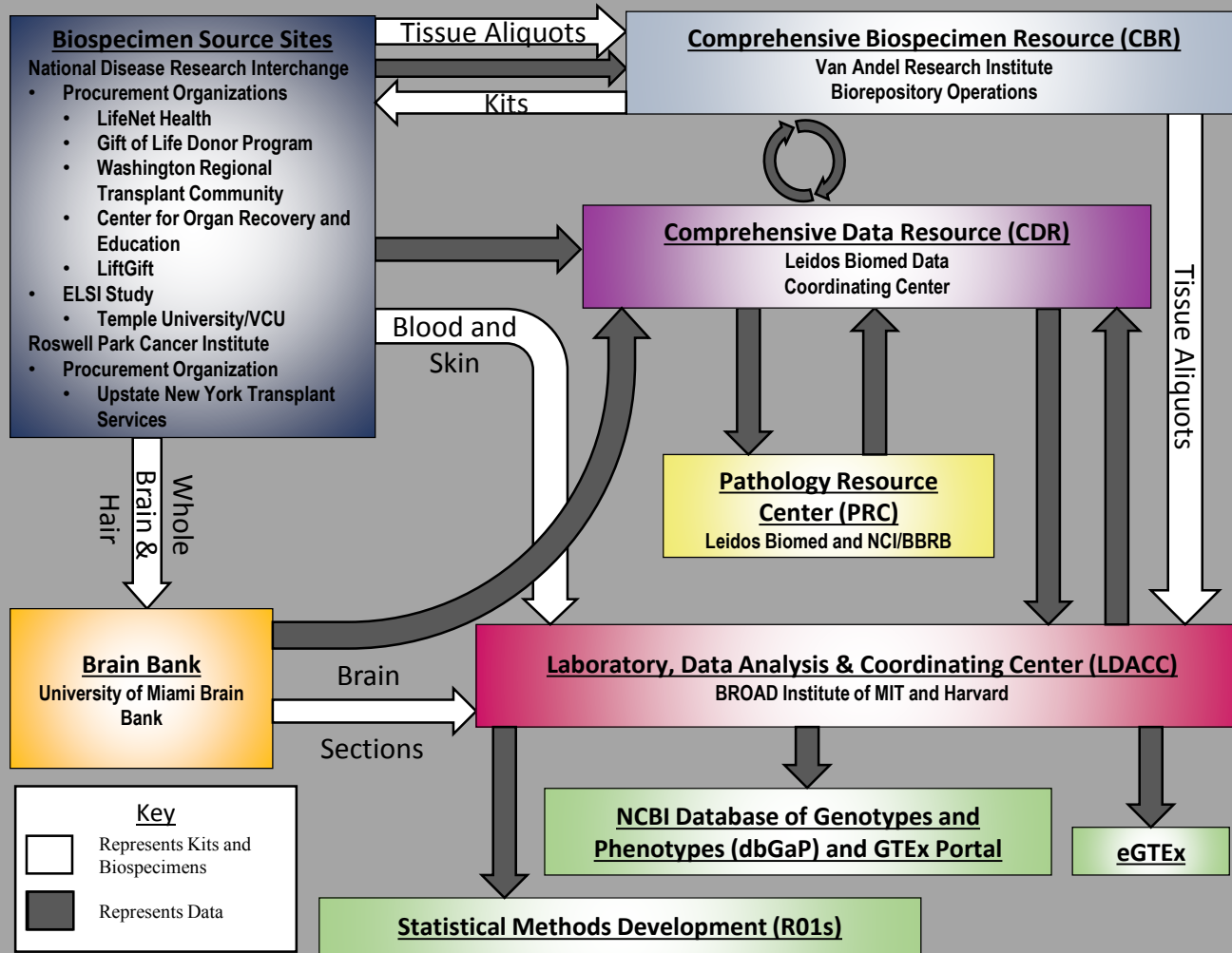
Helen Moore, PhD and Abhi Rao, PhD

Biorepositories and Biospecimen Research Branch

It all starts with the donors

- The project depended on many biospecimens from each of many individuals
- GTEx biospecimens came from deceased individuals with permission of family decision makers
- Collections performed in partnership with Organ Procurement Organizations
- Accompanying study of GTEx-associated Ethical, Legal, and Social Implications (ELSI)
- Integral role of many organizations in developing and managing GTEx

GTEx Team: Overview



Special Thanks

NCI BBRB

Phil Branton
Latarsha Carithers
Ping Guan
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Jim Vaught
Carolyn Compton

Leidos Biomedical Research, Inc.

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Liqun Qi
Karna Robinson
Nancy Roche
Charlie Shive
Anna Smith
Leslie Sobin
David Tabor

Subcontractors

NDRI - Jeff Thomas, Alisa McDonald
and team

Roswell Park Cancer Institute -
Barbara Foster, Mike Moser and team

VARI - Scott Jewell, Dan Rohrer,
Dana Valley and team

Science Care, Inc. - Harold Magazine,
John Fleming and team

Frederick National Laboratory for
Cancer Research - Yelena Golubeva,
Andy Warner and team

Temple University/VCU - Laura
Siminoff, Maghboeba Mosavel, Laura
Barker and team

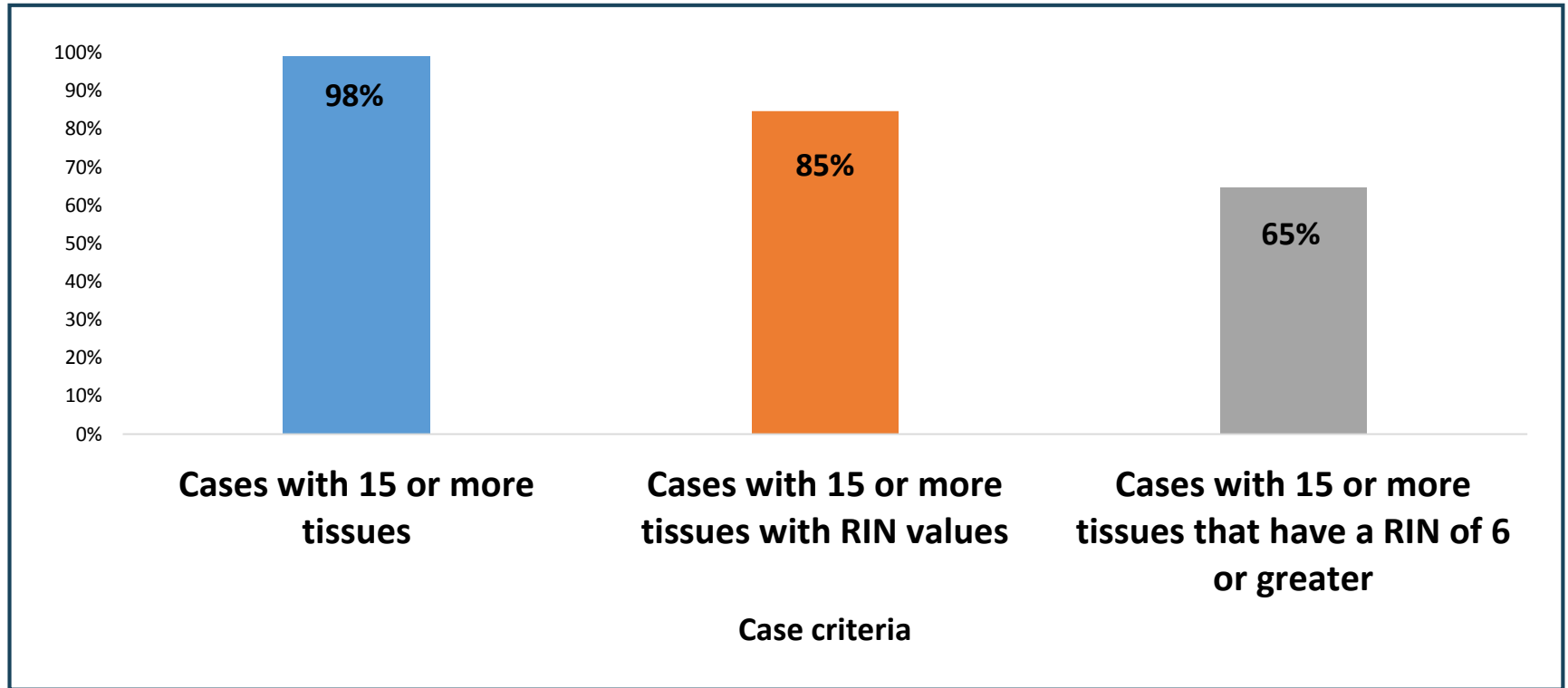
Broad Institute - Kristin Ardlie, Ellen
Gelfand and team

Thank you to the donor families



GTEx Technical Program Goal:

Establish a collection where 70% of all cases have 12 or more tissues with RIN values ≥ 6.0



GTEEx Collection Final Update

- Total collection goal: **965 donors**
- Collections complete as of December 31st, 2015; **965 donors**
- 538 non-brain and 427 brain cases
 - Average PMI for non-brain case: **6.06 hrs**
 - Average PMI for brain case: **15.44 hrs**

GTEEx Case Definitions

Criteria	Definitions and notes
Ineligible cases	Cases that did not pass all eligibility criteria defined in the protocol. Deviation reports were created for each case and reviewed. These cases were accepted by the NIH as part of the GTEEx study.
Case NOT eligible for analysis	Cases that were deemed by the Pathology Review Committee (PRC) review to be diseased or abnormal for an entire case.
Documented cases with history of sepsis	Cases where the source documentation (medical history) indicate sepsis, toxemia or bacteremia. Except for cases deemed not eligible for analysis (see above), the PRC did not recommend exclusion of the case from molecular analysis. Note: Sepsis is <i>NOT</i> an eligibility criteria for the GTEEx study

Final GTEx Collection Numbers

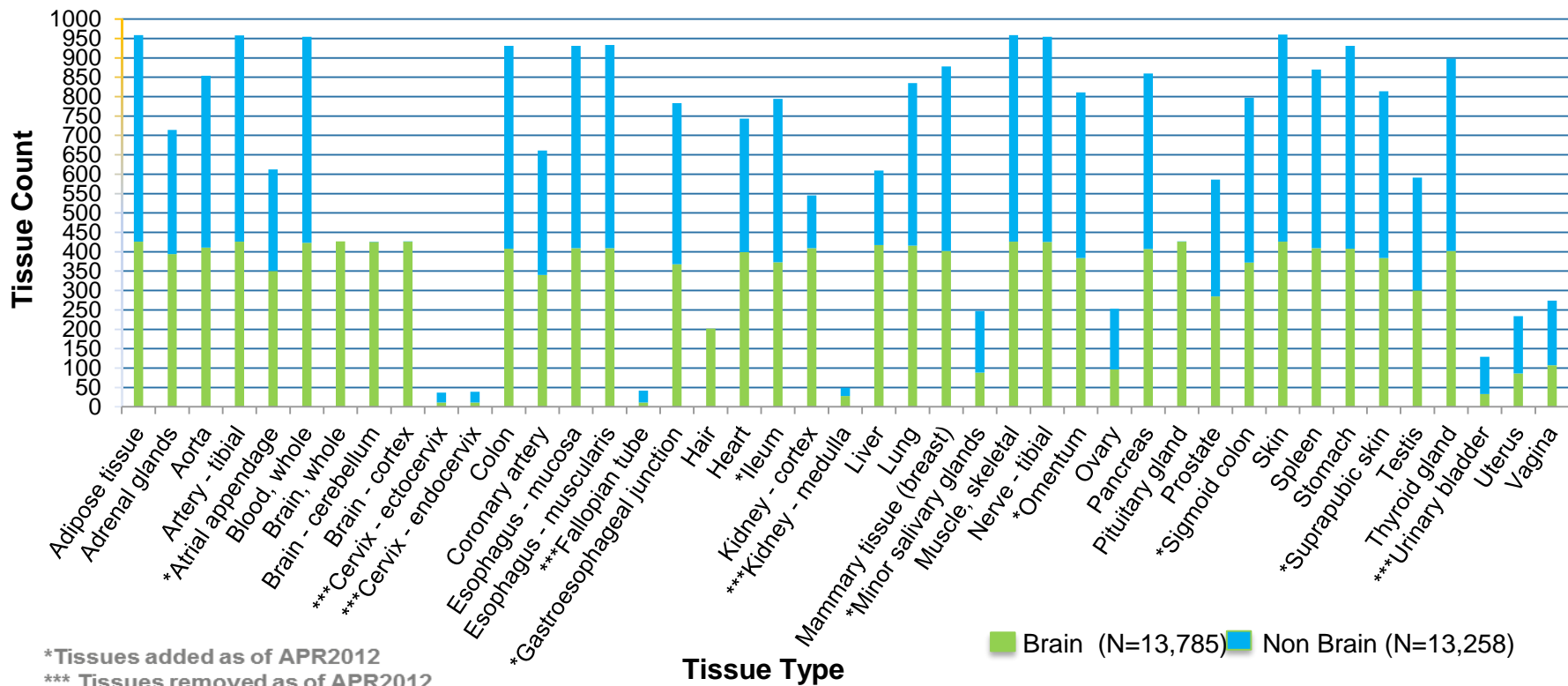
Study	Requirement	Completed	Breakdown	
GTEx Post Mortem Collections <i>(includes ENCODE and BMS donors)</i>	965	965	Brain collected	427
			Brain not collected	538 (237 of which had frozen aliquots collected)
GTEx Surgical Donors	*16 <i>(100 initially)</i>	16 <i>(includes 1 ineligible HCV case which was returned to BSS)</i>		
GTEx/ENCODE	4	4		
GTEx/BMS	32	32		

* Study was terminated early due to low enrollments; 1 ineligible case included in number

Breakdown of GTEx Cases

Criteria	# of cases	Reasons
Ineligible cases	11	<ul style="list-style-type: none">• Includes 1 surgical case that was invalidated (due to HCV)• Age (1 case; < 21.0 yrs.)• BMI (4 cases; > 35.00)• Inadequate number of minimum 5 core tissues collected (4 cases)• IV drug history (1case)
Cases later deemed NOT eligible for analysis	8	<ul style="list-style-type: none">• Acute sepsis (5)• Lymphoma (2)• 1 Surgical case included (due to HCV, same case as above in 'Ineligible cases')
Documented cases with sepsis	30	Information recorded on Clinical Case report form, medical conditions or in note sections (number includes 5 acute sepsis cases above, remaining 25 cases remain eligible as history of sepsis was not exclusionary)

Number of Tissues Collected *~27,000 Tissues and > 69,000 Aliquots*

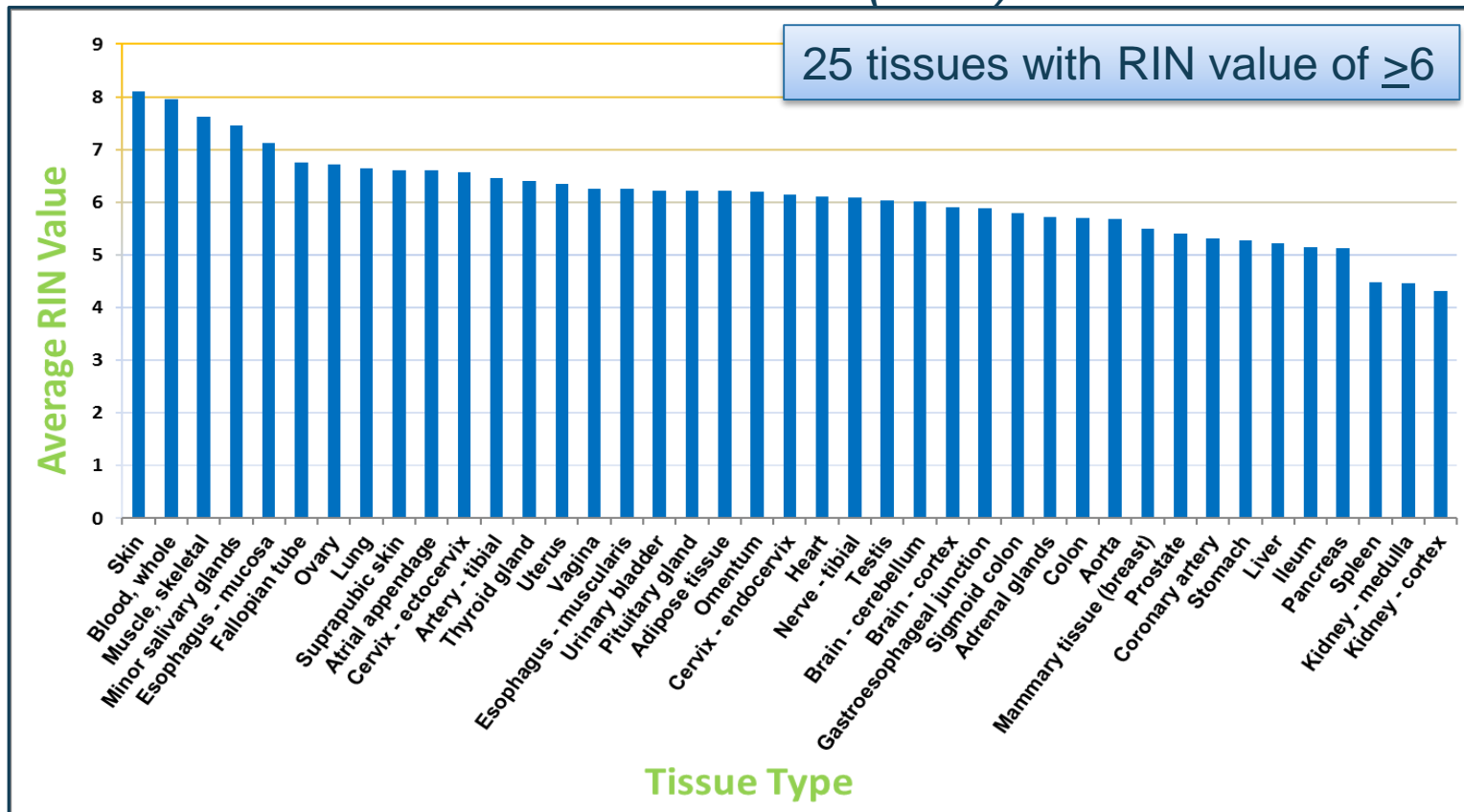


*Tissues added as of APR2012

*** Tissues removed as of APR2012

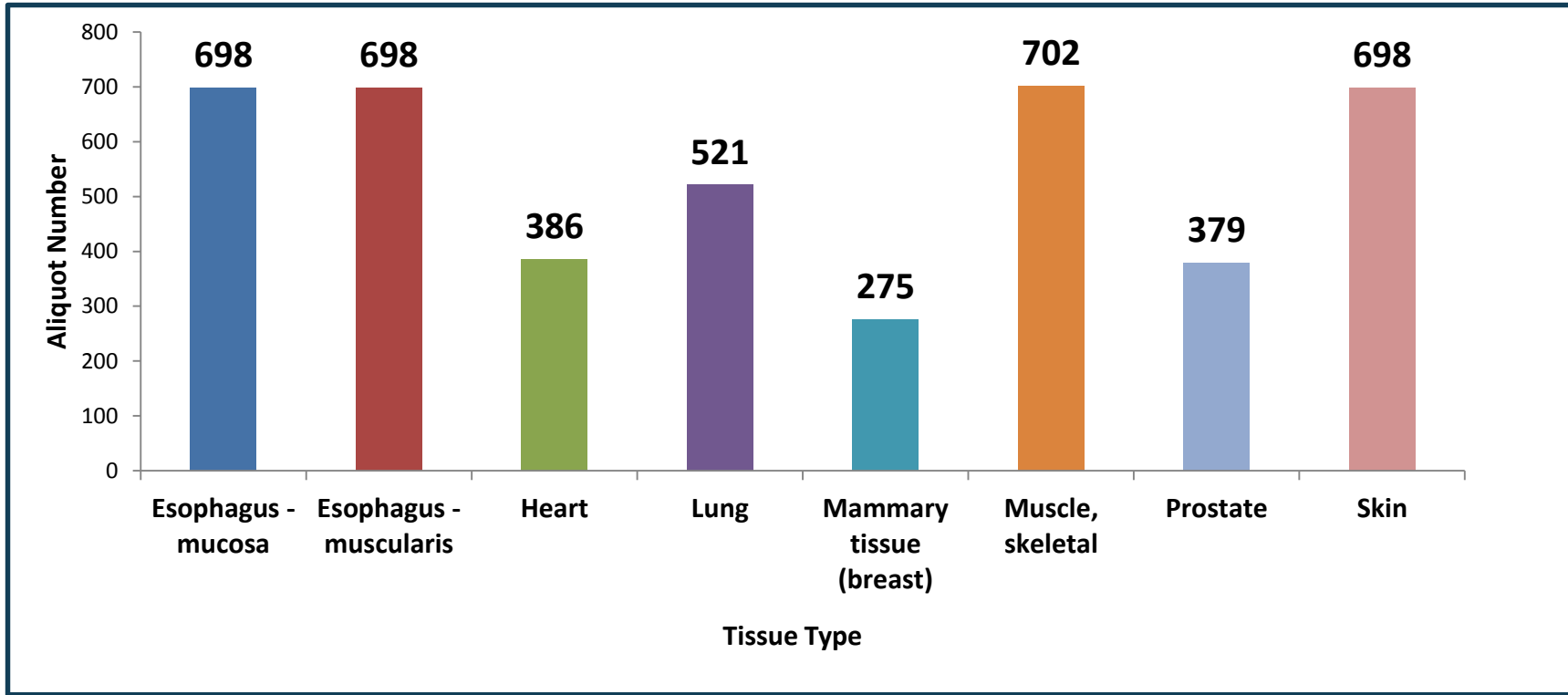
Average RIN by Tissue Type

Cases with RIN values available as of 08.02.2016 (N=855)



Number of Frozen Tissue Aliquots by Tissue Type

(237 cases, 4,357 aliquots, 8 tissue types)



- Frozen fresh on Dry Ice and stored in LN2
- Total of 237 cases with matching frozen tissues to PAXgene preserved tissues

GTEEx Legacy Collection

- **Consolidation** of all GTEEx biospecimens and derivatives under one management plan.
- Transition the responsibility of **biospecimen governance and granting specimen and data access**
- Enhance public **web portal interface** for access to the GTEEx inventory and enable search capability via queries performed on publically available GTEEx data elements.
- Provide a **quality plan** that encompasses oversight of the entire collection with particular focus on ensuring proper transfer and long term maintenance of the specimens.
- Perform **outreach efforts to engage the research community** in understanding the value and opportunities for further research on the GTEEx collection.

Status of GTEx Collection

Collection moved from VARI to the Broad Institute October, 2016

Processing Type	Location	Number of cases	~Number of Specimens
PAXgene-Fixed	Processed at CBR; sent to LDACC	965	31,845
PAXgene-Fixed Paraffin Embedded	CBR	965	31,845
PFPE slides	CBR	965	31,845
Frozen	CBR	230	4,140
BMS (PFPE blocks/slides and LN2/-80 frozen tissue)	CBR	32	645 PFPE blocks 644 frozen tissue (-80°C) 644 frozen tissue (LN2) 1,922 slides
*Whole Brain, unfixed	Miami Brain Bank	436	436

Resources for the Scientific Community:

1. **GTEx Histological Image Viewer:**

https://biospecimens.cancer.gov/resources/tissue_image_library.asp

2. **SOPs from GTEx Biospecimen Collections:**

<https://biospecimens.cancer.gov/resources/sops/library.asp>

3. **GTEx Common Data Elements/Biospecimen Controlled Vocabulary:**

<https://cde.nlm.nih.gov/cde/search?selectedOrg=NCI-GTEx>

4. **Comprehensive Data Resource (CDR) and CDR-Lite:**

<https://github.com/NCIP/CDR-Lite>

5. **Access to Residual GTEx Biospecimens:**

<http://www.gtexportal.org/home/samplesPage> and <https://specimens.cancer.gov/>

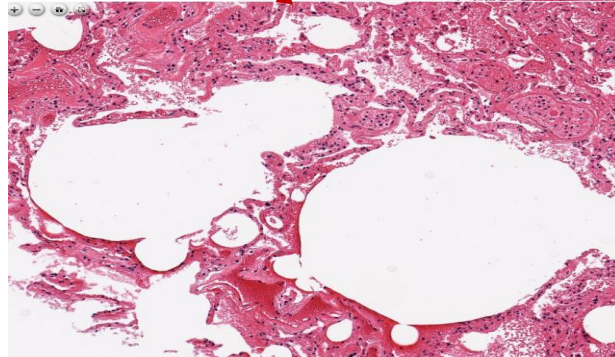
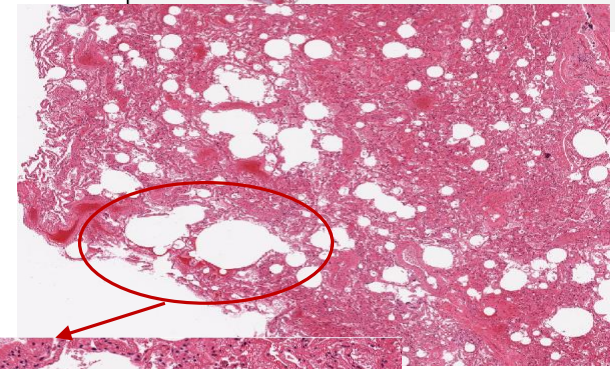
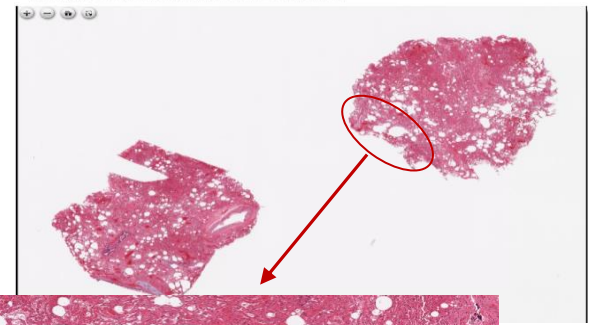
GTEx Histological Images

- Accessible for the public at:
 - https://biospecimens.cancer.gov/resources/tissue_image_library.asp , and
 - <https://commonfund.nih.gov/gtex/data>
- Open access with various search options
 - Specific field search:
 - IDs (case & specimen)
 - Tissue type
 - Autolysis score
 - Age range
 - Gender
 - Acceptability
 - All field search: combination of text and wildcard
- View image with zooming capability without installing image software

Search Results and Viewing

Aperto Slide For Specimen GTEX-111FC-1126 [Print this page](#)

Case ID: GTEX-111FC
 Age Group: 61-70
 Gender: Male
 Tissue Type: Lung
 Autolysis: 1
 Acceptability: Acceptable
 REC Comments: 2 pieces, one piece includes large vessel and focus of cartilage, congestion



National Cancer Institute at the National Institutes of Health | www.cancer.gov

BRD Biospecimen Research Database | **BBRB** Biorepositories and Biospecimen Research Branch | **CDP** Cancer Diagnosis Program | **DCTD** Division of Cancer Treatment and Diagnosis

Home Terms BBRB

GTEX Histological Images

Search

Lung

Displaying 25 of 513 results.

Case ID	Age	Gender	Specimen ID	Tissue Type	Autolysis	Pathology Review Comments	Acceptability	Action
GTEX-1117F	61-70	Female	GTEX-1117F-1026	Lung	2	2 pieces, moderate congestion/moderate to marked autolysis	Acceptable	View
GTEX-111CU	61-60	Male	GTEX-111CU-0326	Lung	0	2 pieces, numerous hemosiderin-laden macrophages, patchy bronchopneumonia, focus of cartilage	Acceptable	View
GTEX-111FC	61-70	Male	GTEX-111FC-1126	Lung	1	2 pieces, one piece includes large vessel and focus of cartilage, congestion	Acceptable	View
GTEX-111VG	61-70	Male	GTEX-111VG-0726	Lung	2	2 pieces; chronic passive congestion with fibrosis, emphysema; foreign body giant cells consistent with aspiration	Acceptable	View
GTEX-111YS	61-70	Male	GTEX-111YS-0626	Lung	1	2 small, irregular, fragmented pieces (7x5 & 5x5mm)	Acceptable	View
GTEX-1128S	61-70	Female	GTEX-1128S-0726	Lung	2	2 pieces, diffuse moderate-marked acute/chronic pneumonitis/congestion	Acceptable	View
GTEX-113JC	51-60	Female	GTEX-113JC-1326	Lung	2	2 pieces; moderate vascular congestion	Acceptable	View
GTEX-117XS	61-70	Male	GTEX-117XS-0326	Lung	3	2 pieces, one piece 90% necrotic/autolyzed, second shows marked congestion and hemorrhage	Unacceptable	View
GTEX-117YW	51-60	Male	GTEX-117YW-0526	Lung	1	2 pieces, severe congestion and edema, numerous hemosiderin-laden macrophages	Acceptable	View
GTEX-117YX	51-60	Male	GTEX-117YX-1326	Lung	1	2 pieces; patchy pneumonia	Acceptable	View
GTEX-1192W	61-70	Male	GTEX-1192W-0626	Lung	1	2 pieces, marked congestion/possible hemorrhagic pneumonitis	Acceptable	View
GTEX-1192X	51-60	Male	GTEX-1192X-1326	Lung	3	2 pieces, marked congestion/hemorrhage	Acceptable	View
GTEX-11DXX	61-70	Female	GTEX-11DXX-0626	Lung	0	2 pieces, some emphysematous change, congestion, minute bone marrow embolism	Acceptable	View
GTEX-11DXY	61-70	Male	GTEX-11DXY-1226	Lung	1	2 pieces, hemorrhage and edema	Acceptable	View
GTEX-11DXZ	51-60	Male	GTEX-11DXZ-0726	Lung	0	2 pieces, numerous hemosiderin-laden macrophages and interstitial pneumonitis with pneumocyte hyperplasia and fibroblast proliferation	Acceptable	View

Image Download Function

Single Image

Home Terms BBRB

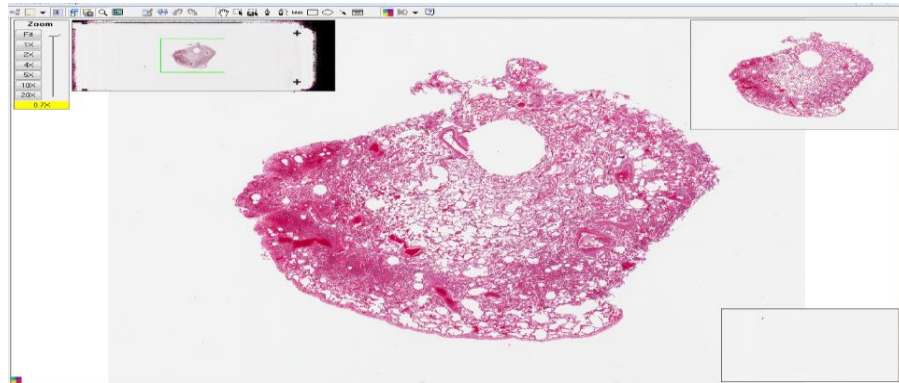
GTEx Histological Images

Search

LUNG

Displaying 25 of 513 results.

Case ID	Age	Gender	Specimen ID	Tissue Type	Autolysis	Pathology Review Comments	Acceptability	Action
GTEX-15EOM	21-40	Female	GTEX-15EOM-0926	Lung	1	2 pieces; over-sized and poorly fixed, includes pleura (not target)	Acceptable	
GTEX-15ER7	21-40	Female	GTEX-15ER7-0926	Lung	1	2 pieces; mild congestion and edema	Acceptable	
GTEX-15ETS	41-50	Female	GTEX-15ETS-1226	Lung	1	2 pieces, pronounced chronic congestion, mild active pneumonitis/bronchitis. bronchial hyaline cartilage present, delineated	Acceptable	



Aperio Slide For Specimen GTEX-N7MS-0926

Case ID: GTEX-N7MS
 Age Range: 61-70
 Gender: Male
 Tissue Type: Lung
 Autolysis: 2
 Acceptability: Acceptable
 PRC Comment: OK for analysis

Do you want to open or save GTEX-N7MS-0926.svs from brdqa.ncifcrf.gov?

GTEx Histology Images

ARTICLE

Complex Sources of Variation in Tissue Expression Data: Analysis of the GTEx Lung Transcriptome

Matthew N. McCall,^{1,*} Peter B. Illei,² and Marc K. Halushka^{2,*}

The sources of gene expression variability in human tissues are thought to be a complex interplay of technical, compositional, and disease-related factors. To better understand these contributions, we investigated expression variability in a relatively homogeneous tissue expression dataset from the Genotype-Tissue Expression (GTEx) resource. In addition to identifying technical sources, such as sequencing date and post-mortem interval, we also identified several biological sources of variation. An in-depth analysis of the 175 genes with the greatest variation among 133 lung tissue samples identified five distinct clusters of highly

The American Journal of Human Genetics 99, 624–635, September 1, 2016

Conducted a study to capture the complex and diverse sources of tissue heterogeneity, specifically histologic and histopathologic characterization in a 'normal' lung tissue dataset.

Standard Operating Procedures (SOPs)

The screenshot shows the BBRB (Biorepositories and Biospecimen Research Branch) website. The header includes the NCI logo, the text 'National Cancer Institute', and 'U.S. National Institutes of Health | www.cancer.gov'. Below the header are logos for CDP (Cancer Diagnosis Program) and DCTD (Division of Cancer Treatment and Diagnosis). A search bar is located in the top right. A navigation menu includes 'Home', 'About BBRB', 'Programs', 'Best Practices', 'News and Events', 'Public Resources', and 'Patient Corner'. The main content area is titled 'Public Resources | Standard Operating Procedures (SOPs)' and 'Last Updated: 07/17/15'. The central heading is 'GTEx Standard Operating Procedures Library' with a note: 'The Entire SOP Library can be downloaded at the bottom of the page.' The content is organized into four sections: A. Enrollment and Informed Consent (5 items), B. Regulatory Procedures for GTEx (3 items), C. Biospecimen Collection for GTEx (6 items), and D. Biospecimen Collection Supplies and Shipping Procedures for GTEx (3 items). A sidebar on the left contains a 'Main' menu with links to 'Tissue Image Library', 'Standard Operating Procedures (SOPs)', 'NCI Biospecimen Evidence-Based Practices', 'Biobank Economics Modeling Tool', 'Recommendations, Templates, and Other Resources', 'Scientific Publications', 'Workshop Summaries and Reports', 'Brochures and Educational Materials', and 'External Resources'. A right sidebar is titled 'Standard Operating Procedures (SOPs)' and includes 'Introduction', 'The NIH GTEx Project', 'Reasons Behind caHUB SOP Release', 'Important Notes on SOPs', and 'GTEx SOP Library'.

- Developed for GTEx and available for public guidance
- Cover various operations including:
 - Ethical and regulatory practices
 - Biospecimen collections
 - Data collection
 - Shipping kits and checklists
 - Pathology review

Biospecimen Controlled Vocabulary

- **GTEx and BPV form elements defined in Protégé as Common Data Elements (CDEs)**
 - Form Elements and valid values definitions stored in Protégé
 - Exported to SOLR for display in the CDR
- **Valid Values defined in SOLR for display in CDR:**
 - **Cause of Death**, Source ICD10-CM
 - Synonyms from UMLS
 - **Medications**, source FDA NDC List
 - **Primary Cancer Type**, source PDQ Disease List
 - **Medical Procedures**, source AMA CPT List
 - Synonyms from UMLS
 - **Demographics**

Comprehensive Data Resource (CDR)

- CDR is a web-based information management system that was developed to support two biospecimen programs at NCI:

- GTE_x
- The Biospecimen Preanalytical Variables (BPV) program
- Published code at GitHub (<https://github.com/NCIP/CDR>)

- CDR is being adopted for other NCI programs

- CDR-Lite development

- Published code in GitHub as open source for public access (<https://github.com/NCIP/CDR-Lite>)

- CDR Collaborative Announcement

- Identify collaborative partners who wish to adopt CDR

The screenshot shows the CDR Comprehensive Data Resource website. At the top left is the CDR logo. To the right, there is a 'Most recent CDR activity' section listing three cases: 'Case-1234' on 3/3/2016, '123abc' on 2/8/2016, and 'STEVE-00001' on 11/9/2015. Further right is a user navigation area with 'Welcome, admin', 'Logout', 'Org: Data Coordinating Center', 'Privileges: DM | PRC | LDS', 'Help', and 'Session expires in: 29:40'. Below the header is a navigation bar with 'Back Office', 'Query Tracker', and 'Deviation List'. A yellow notification banner states 'PRC flag enabled. You now have PRC access!'. The main content area features a 'Choose your Destination' section with three options: 'Project Home' (with a DNA helix image), 'PRC Home' (with a histology slide image), and 'DM Home' (with a gear and red flower image).

GTEx Biospecimens in the Specimen Resource Locator (SRL)

<https://www.specimens.cancer.gov/>

- A biospecimen resource database designed to help researchers locate resources that may have samples needed for their investigational use
- Publicly searchable and includes information about biospecimen banks and procurement services



About the Specimen Resource Locator

The Specimen Resource Locator (SRL) is a biospecimen resource database designed to help researchers locate resources that may have the samples needed for their investigational use. This publicly searchable database includes information about biospecimen banks and sample procurement services. The specimens and samples come from non-commercial, either NCI or non-NCI-funded resources. Investigators can search the database and gain access to thousands of specimens of various tumor, organ, and preservation methods.

In the event you are unsuccessful in finding the appropriate specimen resource you may contact the NCI Tissue Expediter, a scientist, who can further assist you. Also, the Tissue Expediter can assist researchers to identify potential collaborators when needed. The NCI and the NCI's SRL do not oversee or take responsibility for the content, quality or data of the specimen collections or resources participating in the SRL.



GTEx

Adrenal Glands

This resource has a service and/or shipping fee.

Collaboration for use of specimens is not required.

Specimen Data

Organ Site
Adrenal Glands

Histology / Tumor Type
Normal

Specimen Type
Autopsy Specimen, Blood, Cell Line, DNA, RNA

Other Specimen Types in this collection (if any)
Not Available

Preservation Type
PaxGene

Available Data

- > Demographic Information
- > Pre-diagnostic Specimen
- > Risk Factors
- > Pathology Report
- > Treatment Information

Type of Collection

- > NIH/NCI

Application Eligibility

- > Academia
- > Government
- > Non-Profit
- > Other
- > Commercial
- > Non-U.S. Organization

Contact Information

Contact: Simona Volpi
Title: GTEx Project
Address: Rockville, MD
Phone: (301) 443-6453
URL: <https://commonfund.nih.gov/GTEx/index>
Email: simona.volpi@nih.gov



Found 36 matching collections from 1 resource

Click on a collection to view additional details and contact information for the resource.

GTEx

Collection Name	Organ Site	Histology / Tumor Type	Preservation Type
Adipose	Adipose	Normal	PaxGene
Adrenal Glands	Adrenal Glands	Normal	PaxGene
Aorta	Aorta	Normal	PaxGene
Artery	Artery	Normal	PaxGene
Bladder	Bladder	Normal	PaxGene
Blood	Blood	Normal	PaxGene
Brain	Brain	Normal	PaxGene
Breast	Breast	Normal	PaxGene
Cervix Uteri	Cervix Uteri	Normal	PaxGene
Colon	Colon	Normal	PaxGene
Esophagus	Esophagus	Normal	PaxGene
Fallopian Tube	Fallopian Tube	Normal	PaxGene
Hair	Hair	Normal	PaxGene
Heart	Heart	Normal	PaxGene
Kidney	Kidney	Normal	PaxGene
Large Intestine	Large Intestine	Normal	PaxGene
Liver	Liver	Normal	PaxGene
Lung	Lung	Normal	PaxGene
Muscle	Muscle	Normal	PaxGene
Nerve	Nerve	Normal	PaxGene

GTEEx Sample Request

- Complete 1 form and email to: nhgrigtex@mail.nih.gov
 - GTEEx Biospecimen Access Requests (complete and email)
 - GTEEx Biospecimen Access Policy (review)
 - GTEEx Material Transfer Agreement (sent after approval prior to shipment of samples)
- Authorized requests of GTEEx samples can be found on the GTEEx portal
- Additional samples available include PAXgene-fixed Paraffin-embedded (PFPE) blocks and frozen, stored brain regions



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