

Genotype-Tissue Expression (GTEx) Project Material Transfer Agreement (MTA)

Background

The primary goal of the Genotype-Tissue Expression (GTEx) project is to establish a resource database and associated tissue bank in which to study the relationship between genetic variation and gene expression and other molecular phenotypes in multiple reference tissues and to make this resource broadly available to further medical research.

The GTEx project involved the rapid collection of multiple tissue types from deceased donors. The collection of biospecimens from deceased individuals is not legally classified as human subjects research under 45 CFR 46. However, donor recruitment sites obtained written or telephonic authorization from next-of-kin for participation in GTEx. This was typically done through an addendum or modification to an existing authorization form for research donation of tissues and organs. It includes statements common in consent forms such as the intention to perform genetic analyses, establish cell lines, and to share data with the scientific community (see <https://biospecimens.cancer.gov/resources/sops/library.asp> for example language under Enrollment and Informed Consent section). The GTEx project obtains authorization for broad future research use and unless required by the applicant's Institution, specific IRB review is not required.

Biospecimen acquisition for GTEx was accomplished through contracts issued by the National Cancer Institute's (NCI) Biorepositories and Biospecimen Research Branch (BBRB). Leidos Biomedical Research, Inc., the prime contractor to the NCI, served as the Comprehensive Data Resource. Biospecimen collection and processing were accomplished through Leidos Biomedical Research, Inc., subcontracts to the Biospecimen Source Sites (BSSs) and a Comprehensive Biospecimen Resource (CBR).

There were 3 BSSs involved in the collection of biospecimens: The National Disease Research Interchange (NDRI - Philadelphia, PA), Roswell Park Cancer Institute (RPCI - Buffalo, NY) and Science Care, Inc. (Phoenix, AZ). The BSSs worked with their Organ Procurement Organizations (OPOs), American Association of Tissue Bank (AATB) partners and rapid autopsy programs to accomplish recruitment.

At the CBR (The Van Andel Institute, Grand Rapids, MI), an aliquot from each tissue sampled at the BSSs was accessioned, quality controlled, paraffin embedded, sectioned, and stained for histopathology analysis. A second immediately adjacent aliquot was also accessioned, preserved, and set to the LDACC (Laboratory, Data Analysis and Coordination Center) to be used as the primary aliquot for molecular analyses.

Whole brains with attached brain stem and cervical spinal cord, when possible, were shipped from the BSSs to an NIH-funded Brain Bank (University of Miami School of Medicine Brain Endowment Bank, Miami, FL). After sectioning at the Brain Bank, frozen samples from several anatomical regions of the brain were analyzed for gene expression at the LDACC and the remaining brain was banked for future use.

The LDACC, funded through a contract to The Broad Institute, Cambridge, MA, managed by Leidos Biomedical Inc., performs numerous activities, including molecular analysis. The LDACC is responsible for genotype sequencing of blood samples as well as performing RNA-seq of high quality tissues. In addition, it develops, houses, and maintains databases to track, store, and provide access to the GTEx data that includes clinical, collection, handling and processing data (for open access data) as well as submission of all protected, deidentified GTEx data to the database of Genotypes and Phenotypes (National Center for Biomedical Information's (NCBI) dbGaP - for controlled access data). The LDACC is also a member, together with the statistical analysis investigators, of the GTEx Analysis Working Group (AWG), which is responsible for analyses of the integrated data sets.

The use of GTEx biospecimens and any modified and/or unmodified derivatives are subject to the terms of this MTA.

Material Transfer Agreement

This Material Transfer Agreement (the “Agreement”) is by and between The Broad Institute, Inc. (“PROVIDER” or “PROVIDER ORGANIZATION”) and Recipient Scientist, at (“RECIPIENT” or “RECIPIENT ORGANIZATION”).

WHEREAS, the LDACC, the Laboratory, Data Analysis and Coordinating Center, at the Broad Institute has administrative oversight of the GTEx legacy samples and therefore will handle the approval and tracking of all Material Transfer Agreements (MTAs) involving GTEx biospecimens.

WHEREAS, the PROVIDER, the LDACC, has approved the request to transfer biospecimens and related data to the Recipient Scientist for the research purposes identified herein.

NOW, THEREFORE, the PROVIDER and RECIPIENT ORGANIZATION, acting on behalf of the Recipient Scientist, agree as follows:

1. Throughout this Agreement, PROVIDER and RECIPIENT ORGANIZATION are collectively referred to as the “Parties.” This Agreement will become effective upon the date of the last signature affixed below.
2. The following biospecimens and/or modified and/or unmodified Derivatives (“MATERIAL”) and the following data (“DATA”) shall be transferred to RECIPIENT ORGANIZATION:

The above MATERIAL and DATA are the property of the PROVIDER and are made available to RECIPIENT SCIENTIST and RECIPIENT ORGANIZATION as a service to the research community. Researchers accessing the materials may be charged on a cost recovery basis.

3. Definitions. The following definitions, which derive from the Uniform Biological Materials Transfer Agreement (UBMTA), shall apply herein:
- a. Unmodified derivatives: Substances created by the RECIPIENT which constitute an unmodified functional subunit or product expressed by the MATERIAL provided under this Agreement. Some examples include, without limitation: subclones of unmodified cell lines, purified or fractionated subsets of the MATERIAL, proteins expressed by DNA/RNA isolated from MATERIAL, or monoclonal antibodies secreted by a hybridoma cell line created using MATERIAL.
 - b. Modifications: Substances created by the RECIPIENT which contain or incorporate all or part of the MATERIAL, including but not limited to induced pluripotent stem cells (iPSC) and their subsequently derived cell lines, and transfected cells.
4. The MATERIAL and DATA are not for use in human subjects or for the treatment or diagnosis of human subjects or patients.
5. The MATERIAL and DATA provided by the PROVIDER will be de-identified and all Protected Health Information (PHI), as defined by the Federal Health Insurance Portability and Accountability Act (HIPAA, 45 C.F.R. 164), will have been removed.
6. The MATERIAL and/or DATA, including modified and unmodified derivatives, will not be further distributed to others without the PROVIDER's written consent. The RECIPIENT shall refer any request for the MATERIAL to the PROVIDER. To the extent supplies of MATERIAL are available, the PROVIDER may make the MATERIAL available, under a separate agreement.
7. The RECIPIENT agrees that the MATERIAL and DATA will only be used for the stated research purposes as described in the grant application or in the sample access request. Any changes to proposal or research procedure must be reported to the PROVIDER.
8. The RECIPIENT agrees to acknowledge the source of the MATERIAL and/or DATA in any presentation, disclosures, or publications resulting from any analyses conducted on the specimens in accordance with the Publication Policy at <http://www.gtexportal.org>
9. Any MATERIAL and DATA delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. The PROVIDER makes no representations and extends no warranties of any kind, either expressed or implied. There are no express or implied warranties of merchantability or fitness for a particular purpose, or that the use of the material will not infringe any patent, copyright, trademark, or other proprietary rights. Unless prohibited by law, RECIPIENT assumes all liability for claims for damages against it by third parties which may arise from RECIPIENT's use, storage or disposal of the MATERIAL and DATA except that, to the extent permitted by law, the PROVIDER shall be liable to the RECIPIENT when the damage is caused by the gross negligence or willful misconduct of the PROVIDER.
10. The RECIPIENT agrees to use the MATERIAL and DATA in compliance with all applicable statutes and regulations.

11. The MATERIAL and DATA may be provided on a cost recovery basis solely to reimburse the PROVIDER for its preparation and distribution costs. If a fee is requested, the amount will be indicated here:
12. The RECIPIENT shall not attempt to obtain information identifying the donors who donated the MATERIAL.
13. The RECIPIENT agrees to destroy any unused MATERIAL and DATA associated no later than 1 year from the completion of the project unless otherwise instructed by the PROVIDER.
14. The RECIPIENT agrees to prompt publication in agreement with the GTEx publication policy (see <https://gtexportal.org/home/documentationPage#staticTextPublicationPolicy>) and placing of research results derived from the MATERIAL in the public domain. All protected, identifiable data, such as genotype data or RNA seq data, must be deposited in a protected database such as dbGaP. An example is described in the “Resource Sharing Plan” section of RFA-RM-12-009 (<http://grants.nih.gov/grants/guide/rfa-files/rfa-rm-12-009.html>; see also Appendix A).
15. The RECIPIENT agrees that no Intellectual Property (IP) rights are granted to any MATERIALS.
16. Either Party may terminate this Agreement for any reason upon thirty (30) days written notice to the other Party.
17. This Agreement and any amendment hereto may be executed in counterparts and all such counterparts taken together shall be deemed to constitute one and the same instrument. If this Agreement is executed in counterparts, no signatory hereto will be bound until all the Parties named below have duly executed a counterpart of this Agreement.

[The remainder of this page is intentionally left blank. Signature page follows.]

PROVIDER INFORMATION and AUTHORIZED SIGNATURE

Provider Authorized Signatory Name and Title:

Provider Organization: The Broad Institute, Inc.

Address for the Notices Sent by U.S. Postal Service, FedEx, UPS, and Other Couriers to Provider

The Broad Institute, Inc.

Attn.: General Counsel

415 Main Street

Cambridge, MA 02142

T (617) 714-7000

Printed name and signature of Authorized Official

Date

RECIPIENT INFORMATION and AUTHORIZED SIGNATURE

Printed name and signature of Authorized Official

Date

Address for Legal Notices sent to Recipient Organization:

Address for Notices sent to Recipient Scientist:

Appendix A

[RFA-RM-12-009](#) (Funding Opportunity Announcement entitled “Enhancing GTEx with Molecular Analyses of Stored Biospecimens”)

<http://grants.nih.gov/grants/guide/rfa-files/rfa-rm-12-009.html>

Resource Sharing Plan

Individuals are required to comply with the instructions for the Resource Sharing Plans (Data Sharing Plan, Sharing Model Organisms, and Genome Wide Association Studies (GWAS)) as provided in the SF424 (R&R) Application Guide, with the following modifications:

Data Release Principles and Standards. Data from this FOA are expected to be shared in an easily accessible format to increase the value of the significant public investment. Consistent with achieving the goals of this program, the NIH expects that information such as data syntheses, study protocols, bioinformatics tools, and any other meta data collected will be widely shared with the scientific community for research and made publicly available through the GTEx data portal and other data repositories.

Applicants should indicate their willingness to cooperate with the GTEx Consortium and other stakeholders in the development and design of research and standardization methods, procedures, policies and strategies to be applied for this resource. Applicants should also describe prior experience in working as part of a research consortium, developing consensus approaches for data sharing and other research-related topics, or other collaborative activities to meet individual study and collaborative goals.

Data sharing plan. All controlled access data generated from GTEx samples are expected to be deposited into dbGaP (<http://www.ncbi.nlm.nih.gov/sites/entrez?db=gap>) or other NIH Trusted Partners databases. All data without privacy concerns are expected to be returned to the GTEx portal (www.broadinstitute.org/gtex) and other appropriate repositories with open access.

Rapid deposition of data into repositories is expected. Depending on the type of data, the duration of data production, as well as the quantity of the samples assayed in a given period, the frequency of data deposition might vary. All data are expected to be deposited once data generation is completed. Before this and other data deposits, a period of quality control of up to 3 months might be needed. Interim or periodic deposition might be expected if the data are produced over an extended period of time (e.g. >12 months) and are of sufficient size. For example, in a study generating results on a large number of samples over an 18 month period, data deposition may be expected at regular intervals.

NIH does not anticipate a publication embargo. However, a holding period of up to 6 months after each deposit might be considered before the data are made publicly available. This policy

might be revised should an NIH-wide data sharing policy be issued (see <http://grants.nih.gov/grants/guide/notice-files/NOT-HG-10-006.html>).

Applicants should provide a specific proposal for release of data, and are encouraged to address the issue of frequency of the release, based on practical considerations or previous experience and the recommendations above. The reasonableness of the proposed data sharing plan will be assessed by the reviewers.

As is the case for SNP genotyping and RNA-seq data as well as Whole Genome Sequencing and Exome Sequencing data already produced by GTEx, similar data generated in this FOA that contains extensive genetic variation information (e.g., genome-wide methyl-seq) are expected to be deposited into the controlled access part of dbGaP or other NIH Trusted Partners databases. Applicants should address whether they anticipate any of their data requiring controlled access.