Acquisition of Normal Tissues for the GTEx Program

Helen M. Moore

IN 2008, THE U.S. NATIONAL CANCER INSTITUTE (NCI) Biorepositories and Biospecimen Research Branch (BBRB; formerly known as OBBR) began a collaboration with the U.S. National Human Genome Research Institute, the National Institute of Mental Health, and other institutes and centers of the National Institutes of Health (NIH) to develop a new research program called GTEx, or Genotype-Tissue Expression. The goal of GTEx, a program funded by the NIH Common Fund, is to study human gene expression and regulation in multiple human tissues, providing valuable insights into the mechanisms of gene regulation and to better understand how genomic differences may contribute to disease. GTEx planned to analyze multiple human tissues from many different individuals, performing dense genotyping on each individual and analyzing RNA expression within each individual tissue. Genetic variation between individuals would be examined for correlation with differences in gene expression level in different tissues, to identify regions of the genome that influence whether and how much a gene is expressed. By treating the expression levels of genes as quantitative traits, variations in gene expression that are highly correlated with genetic variation could be identified as expression quantitative trait loci, or eQTLs. The GTEx program, notably, planned to make all of the resulting data publicly available, providing a unique and invaluable resource for follow on research.

A critical component of the GTEx program was the acquisition and quality control of the large numbers of different human biospecimens needed for the genome analysis pipeline. Because of the requirements for multiple tissues from a single individual, it was necessary to acquire biospecimens from deceased individuals. A reasonably high level of RNA quality was required for the genomic analysis program, with an associated need to minimize post mortem intervals. In addition, each tissue needed to be examined by a pathologist to assess the relative level of disease of the tissue and the individual. It was essential to develop a highly organized approach to the collection, processing, quality control, annotation, and transfer of the biospecimens and associated data.

Recognizing the enormous challenge of obtaining these biospecimens, the NCI convened a group of experts under its cancer Human Biobank (caHUB) program to help shape the approach for the GTEx biospecimen acquisition program. This expert group developed an extensive document that set out recommendations for acquisition of post-mortem tissues for research. A summary of this document is presented in

this issue of *Biopreservation and Biobanking*, with a hyperlink to the full set of recommendations that are available on the BBRB web site.¹ The recommendations cover best practices for acquiring normal or reference biospecimens under a rigorous and ethical framework. The document is focused on recommendations for the United States but may prove to be useful for similar efforts in other countries.

Following these recommendations, BBRB and its partners in the GTEx program worked to develop a successful tissue acquisition program. The program teamed with rapid autopsy programs and organ procurement organizations to collect the biospecimens for GTEx. The complex activities needed for the program include the enrollment and management of biospecimen source sites through competitive procurements, site visits, training and monitoring, and quality management audits; creation of a standardized consent form and MTA; biospecimen research to inform SOPs; design of collection kits for standardized collection and shipping; processing of specimens for histology, imaging, and pathology review; and creation of an IT infrastructure for donor, specimen, and pathology data. In addition, the program incorporates sub-studies of the ethical, legal, and social implications of the program.

Remarkably, the initial goals for the pilot phase of GTEx tissue acquisition have been met with great success and the project has been funded for scale up. By the summer of 2012, the project had collected nearly 4,400 reference human tissue samples from about 175 donors. Each post-mortem donor contributed, on average, 25 different kinds of tissues, including heart, muscle, and skin. The median RNA Integrity Number was >6 for 37 different tissues, based on analysis of the first 97 donors. The Standard Operating Procedures guiding tissue acquisition have been made freely available online at <http://biospecimens.cancer.gov/resources/sops/>. The genomics pipeline for the project is generating a virtual treasure trove of genomic data on reference tissues that will be available on publicly accessible databases such as the National Library of Medicine's National Center for Biotechnology Information (NCBI) database of Genotypes and Phenotypes (dbGaP) (http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000424) and the GTEx Data Portal (<http://www.broadinstitute.org/gtex>). The first publications from the GTEx program are in preparation and expected to be published in 2013.

BBRB and its partners in the GTEx program are pleased to be able to share the summary of recommendations with the

U.S. National Cancer Institute, Bethesda, Maryland.

readers of *Biopreservation and Biobanking*. Normal or reference biospecimens are an essential comparator tissue for studies of human disease and are often extremely difficult to obtain. It is our hope that the recommendations set out by this group of experts will be helpful to biobankers and researchers worldwide in their efforts to procure and provide high quality biospecimens and associated data collected in an ethical framework. We thank the many individuals and organizations who have contributed to the success of this project.

Reference

1. Mucci N, Moore H, Brigham L, Goldthwaite C, Little A, Lockhart N, Scott M, Struewing J, Vincent S, Compton C [cancer Human

Biobank (caHUB) Acquisition of Normal Tissue Subgroup, National Cancer Institute]. Meeting Research Needs with Postmortem Biospecimen Donation: Summary of Recommendations for Postmortem Recovery of Normal Human Biospecimens for Research. *Biopreserv Biobank* 2013;11:77–82.

Address correspondence to:

Helen M. Moore, Ph.D.

National Cancer Institute

11400 Rockville Pike, Suite 700

Bethesda, MD 20892-2590

E-mail: moorehe@mail.nih.gov