# The Cancer Genome Atlas (TCGA) Pilot Project

## Charting a new course for prevention, diagnosis, and treatment of cancer

Every day more than 1,500 Americans die from cancer — about one person every minute. As the U.S. population ages, this rate is expected to rise significantly unless researchers can develop new strategies to stop the growth and spread of cancer cells within a patient.

Among the most promising strategies are efforts to identify key genetic “targets” within cancer cells and then create therapeutics to zero-in on those targets. This approach for attacking cancer through its genetic vulnerabilities stems from recent advances made possible by the sequencing of the human genome.

Building upon the foundation laid by researchers, the National Institutes of Health (NIH) launched The Cancer Genome Atlas (TCGA) Pilot Project to further scientific understanding of cancer and create a comprehensive “atlas” of the genomic changes involved in cancer.

The Pilot Project is a three-year collaboration of NIH’s National Cancer Institute (NCI) and National Human Genome Research Institute (NHGRI).

Today, scientists at institutions across the nation are collaborating on the Pilot Project. Using innovative tools and technologies, they are working together in a coordinated, systematic manner to create an atlas of genomic changes in three specific cancers: brain, lung, and ovarian.

### TCGA May Help Define the Future of Cancer Research

Scientific understanding of the molecular roots of cancer is improving daily. However, cancer is an extremely complex disease and, from a genetic standpoint, may someday prove to be unique for each cancer patient. Scientists expect that a deeper, systematic exploration of cancer will provide important insights into the mechanisms responsible for the uncontrolled growth of cancer cells and their spread throughout the patient’s body.

Data from the Pilot Project will provide researchers and clinicians with a glimpse of what may grow into a comprehensive atlas of molecular information listing the genomic changes in all types of cancer.

The genomic information generated by TCGA could stimulate advances in cancer research and provide opportunities for the discovery and development of new targets for cancer therapeutics. It could also provide new ways to help clinicians develop personalized treatment plans for each patient and allow clinical trials to focus on patients who are most likely to respond to specific treatments.

### TCGA Starts by Studying Three Cancers

The Pilot Project focuses on three types of cancers: brain (glioblastoma), lung, and ovarian. Together, these cancers account for more than 258,480 cancer cases each year in the United States.

TCGA is starting as a Pilot Project because the approach and infrastructure for a project of this scale have to be tested thoroughly before it is feasible to study a large number of tumors. Brain, lung, and ovarian cancers were selected for the Pilot Project because of the availability of high-quality human tissue collections, known as biorepositories, that met TCGA’s strict scientific, technical, and ethical requirements, and because these cancers have poor prognoses for diagnosed patients.

### What Causes Cancer?

The development of cancer is a multi-step process in the life of a cell. Cancer can be initiated by mutations in a cell’s DNA. DNA molecules in our body contain the genetic information we inherit from our parents. A mutation in DNA is simply a change in DNA. Everyone acquires some mutations to their DNA during the course of their life. These mutations occur through a variety of mechanisms, some inherited and others occur after birth.

All children are born with some genetic mutations that they inherit from their parents. These are called germline mutations. Other DNA mutations occur sporadically throughout our lifetime. These mutations are called somatic mutations. They are sometimes caused by exposure to carcinogens from the environment or from lifestyle choices, such as tobacco use. Somatic mutations are responsible for the vast majority of cancers. The purpose of TCGA is to create an “atlas” of the significant somatic mutations associated with most cancers.

## TCGA Process

Beginning with the critical first step of patient participation, TCGA involves a broad cross-section of the cancer research community, including basic researchers, clinical researchers, bioethicists, doctors, nurses, cancer patients, and advocates.

TCGA is a network of four components, each critical to the success of the project:
• Biospecimen Core Resource
• Cancer Genome Characterization Centers
• Genome Sequencing Centers
• Data Management, Bioinformatics, and Computational Analysis, including a TCGA Data Coordinating Center

Technology development plays a vital role in advancing the efforts of each of the four TCGA components.

The four interacting components of the TCGA Research Network are the:

**Biospecimen Core Resource**
Tissue samples are carefully catalogued, processed, checked for quality, and stored, complete with important medical information about the patient. Samples are coded to remove any descriptors that might connect a sample with the patient’s private information.

**Cancer Genome Characterization Centers**
Several technologies are used to analyze the genetic changes involved in cancer. The genetic changes identified are further studied by the genome sequencing centers.

**Data Management, Bioinformatics, and Computational Analysis**
The information generated by TCGA is centrally managed and entered into the TCGA Data Portal, allowing scientists access to the information throughout the course of the Pilot Project. As new analytical tools are developed, they will be made available to the research community.

**Genome Sequencing Centers**
High-throughput genome sequencing centers identify the changes in the DNA sequence that are associated with specific types of cancer.

**The specific steps in TCGA process are:**

**1. Patient Volunteerism**
Eligible cancer patients are asked to donate tissue and/or blood samples.

**2. Biospecimen Distribution**
A centralized facility processes tissue samples and then sends genetic materials to TCGA research centers.

**3. Research and Discovery**
TCGA components work together to identify genomic changes associated with cancer.

**4. Data Sharing**
Genomic information generated by TCGA is made widely available through public databases. Researchers around the world can use the information to speed advancements in cancer biology and related technologies.

**5. Goals**
Advances made by researchers using TCGA data pave the way for targeted strategies for diagnosing, treating, and preventing cancer.

## How Do NCI and NHGRI Receive Input About TCGA?

A group of outside experts, called TCGA External Scientific Committee, provides input to NCI and NHGRI on all aspects of the Pilot Project.

The committee provides perspectives from all communities, including patient advocates, clinicians, and scientists, and facilitates communication across all communities. Prior to undertaking the project, NCI and NHGRI held a series of meetings to gather input from the scientific and advocacy communities about TCGA. In addition, specific forums are being held to bring together members of TCGA network and experts in brain cancer, lung cancer, and ovarian cancer so they can collaborate as TCGA studies these cancers.

## How Will NCI and NHGRI Evaluate TCGA?

Success factors for the Pilot Project include completion of genomic analysis of the three initial types of cancer, identification of specific alterations in genes associated with cancer, and the ability to differentiate cancer subtypes based on genomic changes.

## In the Future, How May TCGA Improve Diagnosis, Treatment, and Prevention of Cancer?

TCGA data is already generating promising cancer research findings with the first results published from its brain cancer study. TCGA has identified many key gene mutations involved in brain cancer, including three new ones, adding clarity to the complex manner by which the main genes of cancer are expressed. The findings will help researchers better understand the role of genetic pathways in leading to brain cancer. These pathways, or set of interactions, occur between various groups of genes, and are dependant upon each other. Among the most exciting of these results is an unexpected observation of a potential resistance to a common chemotherapy drug, used to treat brain cancer patients.

This improved understanding of genetic changes in cancer may lead to new targets for cancer therapeutics, better tools for assigning patients to clinical trials, and more personalized treatment plans for patients. In time, findings may also improve diagnostics to assess cancer risk, and improve cancer prevention strategies.

## How Can I Get More Information?

For more information about TCGA, including policies, participating institutions, and progress, please visit http://cancergenome.nih.gov.

Or contact us at:

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For more information about the National Cancer Institute and its programs, please visit http://cancer.gov.

For more information about the National Human Genome Research Institute, please visit http://genome.gov.

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