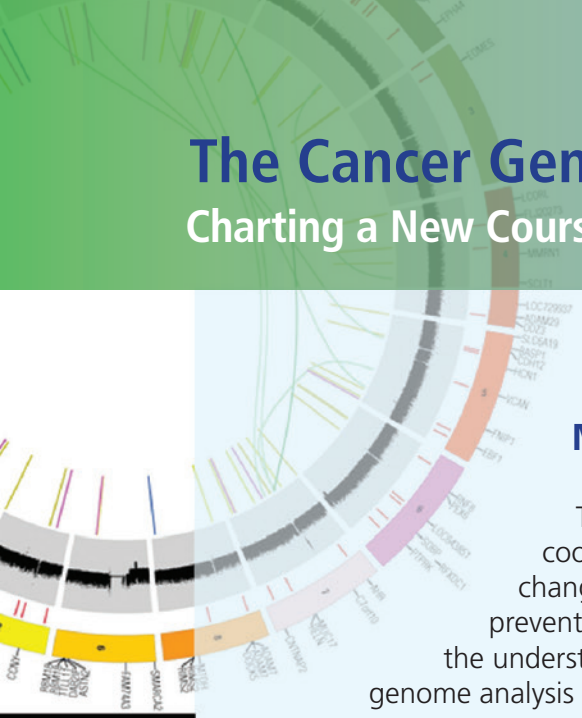
National Cancer Institute
National Human Genome Research Institute

The Cancer Genome Atlas:

Charting a New Course for Cancer Prevention, Diagnosis and Treatment



Mission and Goals

The Cancer Genome Atlas (TCGA) is a comprehensive and coordinated effort to create a detailed catalog, or "atlas," of genomic changes associated with specific types of tumors to improve the prevention, diagnosis and treatment of cancer. Its mission is to accelerate the understanding of the molecular basis of cancer through the application of genome analysis and characterization technologies.

Accomplishments and Expansion of TCGA

TCGA was initiated as a pilot project in 2006 by the National Cancer Institute and the National Human Genome Research Institute, both parts of the National Institutes of Health. Its goal was to comprehensively map and characterize the genomic changes in brain and ovarian cancers, as well as to prove that a national network of researchers could effectively collaborate to generate large-scale genomic data and make discoveries. The achievements of the pilot project led the National Institutes of Health to commit additional resources to TCGA for the characterization of more than 30 additional tumor types, including nine rare cancers. This success of the expansion has inspired the creation of international programs like the International Cancer Genome Consortium, in which TCGA participates.

Benefits of TCGA

TCGA provides the cancer research community with a valuable resource. TCGA has:

- Collected an unprecedented number of high-quality human cancer samples as well as their matching normal tissues, allowing researchers to identify important genomic changes that may play a role in the development of cancer
- Consistently characterized and analyzed each sample, yielding a deeper, more reliable and broader perspective of the cancer genome compared to previous approaches of more limited scope
- Fostered collaborations across broad cross-sections of the cancer research community by making the data freely available in real time

Cancers Selected for Study

The following cancers have been selected for study by TCGA because of their relatively poor prognosis and overall public health impact, as well as the availability of tumor and matched normal tissues that meet TCGA standards for patient consent, quality and quantity.

Breast

- Breast Ductal Carcinoma
- Breast Lobular Carcinoma

Central Nervous System

- Glioblastoma Multiforme
- Lower Grade Glioma

Endocrine

- Adrenocortical Carcinoma
- Papillary Thyroid Carcinoma
- Paraganglioma
- Pheochromocytoma

Gastrointestinal

- Cholangiocarcinoma
- Colorectal Adenocarcinoma
- Esophageal Cancer
- Liver Hepatocellular Carcinoma
- Pancreatic Ductal Adenocarcinoma
- Stomach Cancer

Gynecologic

- Cervical Cancer
- Ovarian Serous Cystadenocarcinoma
- Uterine Carcinosarcoma
- Uterine Corpus Endometrial Carcinoma

Head and Neck

- Head and Neck Squamous Cell Carcinoma
- Uveal Melanoma

Hematologic

- Acute Myeloid Leukemia
- Diffuse Large B-Cell Lymphoma
- Thymoma

Skin

- Cutaneous Melanoma

Soft Tissue

- Sarcoma

Thoracic

- Lung Adenocarcinoma
- Lung Squamous Cell Carcinoma
- Mesothelioma

Urologic

- Chromophobe Renal Cell Carcinoma
- Clear Cell Kidney Carcinoma
- Papillary Kidney Carcinoma
- Prostate Adenocarcinoma
- Testicular Germ Cell Cancer
- Urothelial Bladder Carcinoma

TCGA is no longer accepting additional samples for characterization.

Value of TCGA Data: Cross-Cutting Cancer Analysis

All TCGA samples have been processed in the same manner. This consistency allows for the samples to be compared across cancer types. This research has led to surprising new findings. For example, in TCGA's 2012 paper on breast cancer genomes[1], researchers found that one type of breast cancer showed greater genomic similarity to a subtype of ovarian cancer than to other types of breast cancer.

This finding demonstrates the potential of analyzing and treating tumors based on their genomic characterization, rather than organ of origin. One day, patients may be cared for based on their genomic profile instead of where their cancer originated. For instance, a treatment may be effective for both a uterine carcinosarcoma and one subtype of an esophageal tumor, but not for a second esophageal subtype.

TCGA is uniquely able to facilitate this research because the data have been generated under similar protocols.

[1] The Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumors. *Nature*. Online Sept. 23, 2012. In print Oct. 4, 2012. DOI: 10.1038/nature11412.

The TCGA Research Network: The Process of Genomic Discovery

The TCGA program includes a broad cross-section of the cancer research community. The TCGA Research Network includes scientists, bioinformaticians, bioethicists, doctors, nurses, advocates, and many others.

The TCGA Network consists of four basic components:

Sample Collection and Processing 1

- Samples are gathered and reviewed at Tissue Source Sites (TSSs), and then shipped to the Biospecimen Core Resource (BCR).
- At the BCR, samples are screened by pathologists and other researchers to ensure that each meets TCGA's rigorous standards.
- Analytes (the macro-molecules to be characterized) are extracted from the samples and measured to guarantee sufficient quantity and high quality for the following sequencing and characterization steps.

Genome Characterization 2

- Using the analytes (DNA, RNA, and protein), data are generated at the Genome Characterization Centers (GCCs) and the Protein Characterization Centers (PCCs).
- These components of the TCGA Research Network produce data on: Gene and Protein Expression, DNA Copy Number Alterations, Epigenomics (modifications to DNA which are not inherited, such as methylation), and miRNAs (short RNAs that control gene expression).

Genome Sequencing 3

- The DNA and RNA are also sent to the Genome Sequencing Centers (GSCs) where they undergo sequencing.
- Exome sequencing, or sequencing of all the coding genes, is performed on all cases.
- Some are selected for whole genome sequencing, which is sequencing of the complete genome, both coding and non-coding regions.

Data Management and Analysis 4

- All data are made freely available prepublication.
- Data may be accessed via:
  - Cancer Genomics Hub (CGHub), a database that houses lower level sequence data and alignments.
  - The TCGA Data Portal, where all other data (including some clinical information) are deposited. Most of these data are openly accessible.
- The Genomic Data Analysis Centers (GDACs) develop tools to analyze the immense amount of data generated by TCGA. All tools are publically available.

Towards Precision Medicine

Genomic information is leading the way to more effective diagnosis and treatment strategies that are tailored to a patient's cancer. The application of genomic insight to a therapeutic approach tailored to each patient is known as precision medicine. These therapies can target enzymes that trigger cancer cell proliferation, proteins that regulate gene expression or factors that induce blood vessel growth, among many others. An example of personalized medicine is the drug imatinib (Gleevec), designed to inhibit abnormal tyrosine-kinase activity in chronic myelogenous leukemia. The breast cancer drug trastuzumab (Herceptin) works primarily in HER2 positive cancers, curbing the overactivity of the HER2 pathway. Erlotinib (Tarceva) and gefitinib (Iressa) both target EGFR tyrosine kinase, which is often highly expressed in lung cancer.

The genomic information generated by TCGA lays the foundation upon which similar treatments for other types of cancer may be built.

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