

# The Cancer Genome Atlas (TCGA) Inception and Development Timeline

# September 2003

The National Cancer Advisory Board (NCAB) constituted an Ad Hoc Subcommittee on Biomedical Technology, which would later become an NCAB Working Group on Biomedical Technology.

# NCAB Working Group on Biomedical Technology

<u>Co-Chairs</u> Leland H. Hartwell, PhD, FAACR Eric S. Lander, PhD, FAACR

# September/November 2004

Presentations made to EC and NCI Board of Scientific Advisors (BSA) outlining the proposed TCGA project.

# February 2005

NCAB Working Group on Biomedical Technology recommends creating the Human Cancer Genome Project (HCGP), which would ultimately become The Cancer Genome Atlas (TCGA). The recommendation to establish the group was issued in a report (see below) to the NCAB that was co-authored by Drs. Hartwell and Lander on behalf of the NCAB Working Group on Biomedical Technology.

# Report to the National Cancer Advisory Board

# FINDING CURES TOGETHER

# November 2005

Pilot project approved by NCI Board of Scientific Advisors (BSA) following presentation of proposed program.

# December 2005

The Cancer Genome Atlas Pilot Project announced as a collaboration between the NCI and the National Human Genome Research Institute (NHGRI) via press conference.

# Press Conference Recording

# 2006

• TCGA launched as a 3-year pilot project partnership between NCI and NHGRI to address key questions to determine the feasibility of a full-scale project that will ultimately facilitate the development of a complete "catalogue" of all genetic alterations in cancer.



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- Project Goals:
  - Assemble high quality samples of each type
  - Characterize tumor genome by various approaches
  - Rapidly share data with scientific community
  - Compare and improve technologies
  - Integrate and analyze data to illuminate genetic basis of cancers
- Key questions posed at start of project:
  - o Can samples of adequate quality and quantity be assembled?
  - Can high quality, high throughput data be generated with current platforms?
  - o How sensitive, specific and comparable are current platforms?
  - o How can diverse data sets be integrated and what can be learned from integration?
  - Can recurrent events be distinguished from random background noise?
  - Can we identify new genes associated with cancer types?
  - o Can we identify new subtypes of cancer?
  - O Does new knowledge suggest therapeutic implications?
  - Can a network project drive technology progress in cancer?
- Cancers being investigated:
  - Glioblastoma multiforme
- American Association
- Ovarian Cancer (Serous cystadenocarcinoma)
  Squamous Cell Lung Carcinoma
  - Squamous Cell Lung Carcinoma
- Co-founders:
  - o Anna D. Barker, PhD, Deputy Director, National Cancer Institute
  - Francis S. Collins, MD, PhD, Director, National Human Genome Research Institute

# October-November 2006

NIH announces two initial centers to execute the work of the TCGA.

# 1. Cancer Genome Characterization Centers (CGCCs)

- Broad Institute of MIT and Harvard, Cambridge, MA
- Charge: Identify changes in expression and copy number alterations that occur in cancer.
- Harvard Medical School and Brigham and Women's Hospital, Boston, MA
- Charge: Characterize tumor samples for alterations in chromosome segments copy number.
- Lawrence Berkeley National Laboratory, Berkeley, CA
- Charge: Identify changes in the transcription profiles that occur in cancer.
- Memorial Sloan-Kettering Cancer Center, New York, NY



- Charge: Characterize chromosome segment gains and losses; detect novel genetic rearrangements.
- The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD;
   University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA
- Charge: Detect changes in methylation profiles associated with transcribed genes in cancer samples.
- Stanford University School of Medicine, Palo Alto, CA
- Charge: Identify chromosome segments copy number variation found in cancer.
- University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC
- Charge: Identify changes in the transcription profiles that occur in cancer.

# 2. Data Coordinating Centers

- SRA International, Inc., Fairfax, VA
- National Cancer Institute Center for Bioinformatics, Bethesda, MD
- University of California, Santa Cruz, Santa Cruz, CA

#### Post 2006

Following the creation of the various Cancer Genome Characterization Centers and the formation of a Data Coordinating Center, six additional centers were later developed.

- 1. Genome Sequence Centers (GSCs) 2007
  - Baylor College of Medicine
  - Broad Institute of MIT and Harvard
  - Washington University School of Medicine
- 2. Tissue Source Sites (TSSs) 2007
  - Nationwide Children's Hospital
- 3. Biospecimen Core Resource (BCR) 2009
  - Nationwide Children's Hospital
- 4. Proteome Characterization Centers (PCCs) 2011
  - Vanderbilt University
- 5. Cancer Genomics Hub (CGHub) -2011
  - University of California Santa Cruz
- 6. Genome Data Analysis Centers (GDACs) 2015
  - Broad Institute of MIT and Harvard
  - Buck Institute/ University of California Santa Cruz
  - MD Anderson Cancer Center



# December 2006

First TCGA Steering Committee meeting held.

# February 2007

TCGA Pilot Project status report presented by Dr. Barker at National Cancer Advisory Board Meeting

# September 2008

First TCGA publication released (Nature. 2008 Oct 23;455(7216):1061-8.)

"Comprehensive genomic characterization defines human glioblastoma genes and core pathways"

Corresponding authors: Lynda Chin, MD and Matthew Meyerson, MD, PhD

# February 2009

• President Obama signs the American Recovery and Reinvestment Act (ARRA); NIH-directed funding allocated from this act responsible for sustaining the TCGA project.

# September 2009

- TCGA update presented by Dr. Barker to the National Cancer Advisory Board
- Phase II introduced by Dr. Barker and Dr. Mark Guyer (NHGRI)
- Expanded Project Goals presented:
  - o Establish the needed infrastructure;
  - O Develop a scalable "pipeline" beginning with high quality samples;
  - Determine the feasibility of a large scale, high throughput, systematic approach to identifying all of the relevant genetic alterations in cancer;

for Cancer Research

- O Systematically evaluate up to three cancers using a statistically robust sample set (500 cancers and matched controls);
- Make the data publicly and broadly available to the cancer communities in a manner that protected patient privacy
- TCGA Pilot Project Overall Summary Presented:
  - o Set up and functionalized all part of TCGA network (10 centers, over 150 scientists) and developed pipeline from samples to data availability
  - O Built an unprecedented team of scientists, oncologists, pathologists, bioethicists, technologists and bioinformaticists and a working pipeline from sample to data release



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- o Set a high bar for sample quality and percentage of tumor nuclei which drove data quality
- Implemented 2nd generation sequencing methods Included intensive effort on computational methods; worked NCBI to pioneer controlled access release of human medical sequencing large data sets
- Outcomes to date:
  - Signal can be differentiated from "noise"
  - New cancer genes have been discovered beyond the "streetlamps"
  - Tumor subtypes can be differentiated based on comprehensive knowledge of genomic alterations
  - The integrated teams can be built, and it will take teams to analyze multi-dimensional data
  - Clinically relevant data has/will come from this comprehensive approach
  - High throughput large scale comprehensive characterization is possible and a prerequisite to defining the range and biologic effects of genomic alterations (and their expression) in cancer
  - Single targets unlikely pathway biology in cancer is likely our best hope argues strongly for rational combinations and/or new generations of interventions

# <u>2010</u>

- Phase II of the project initiated by Dr. Barker, TCGA program staff, and pilot phase investigators; included the addition of data analysis centers.
- Phase II structure was maintained through completion of the project in 2018 (33 tumors completed).
- TCGA Phase II Goals:
  - o Project will scale production level pipeline for 20 tumors
  - o Increased emphasis on an analysis pipeline
  - o Integration of next generation genome characterization/sequencing technologies
  - o Specific Phase II goals:
    - Standards and SOPs for biospecimen acquisition high quality of all aspects of samples, clinical information and data
    - Mix of common and rare tumors emphasis on highly lethal tumors focus on subtypes as appropriate
    - Complete genome characterization each cancer case
    - Two levels of data integration and analysis advanced approaches and tools for visualization and management of data
    - Quality management system
- Results from the TCGA Pilot were used to design and scale up the follow-on large scale TCGA project that
  operated from 2009-2018 exceeding goals and providing an unprecedented array of cancer specific data sets
  and a number of seminal findings beyond the original goals.

### November 2011



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The Cancer Genome Atlas Research Network convenes its first open scientific symposium in Washington, DC. TCGA researchers and outside investigators from around the world presented results on the use of TCGA data to make biological discoveries about cancer. This two-day meeting included lectures, collaborative workshops and poster sessions.

# Recorded Lectures

# Meeting Agenda

<u>Co-Chairs</u> Lynda Chin, MD Elaine R. Mardis, PhD, FAACR

# November 2012

On November 27-28, 2012, The Cancer Genome Atlas (TCGA) held its second annual scientific symposium at The Crystal Gateway Marriott in Crystal City, VA. Through collaborative workshops, poster sessions and plenary presentations, TCGA investigators from around the world shared their novel biological discoveries, analytical methods and translational approaches using TCGA data. By this time, TCGA had released data for more than 6000 cases of human cancer, with each case having mRNA/miRNA expression, copy number, promoter methylation, and mutation analysis datasets accessible.

Recorded Lectures
Meeting Agenda

<u>Co-Chairs</u> Matthew Meyerson, MD, PhD Ilya Shmulevich, PhD

for Cancer Research

# May 2014

On May 12-13, 2014, The Cancer Genome Atlas (TCGA) held its third annual scientific symposium at Natcher Conference Center in Bethesda, MD. Through collaborative workshops, poster sessions and plenary presentations, TCGA investigators from around the world shared their novel biological discoveries, analytical methods and translational approaches using TCGA data.

Recorded Lectures and Meeting Agenda

<u>Co-Chairs</u> Marco Marra, PhD Matthew Meyerson, MD, PhD

May 2015



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On May 11-12, 2015, The Cancer Genome Atlas (TCGA) held its fourth annual scientific symposium at Natcher Conference Center in Bethesda, MD. Through collaborative workshops, poster sessions and plenary presentations, TCGA investigators from around the world shared their novel biological discoveries, analytical methods and translational approaches using TCGA data.

By May 2015, TCGA had accrued more than 10,000 cases of human cancer for over 25 different cancer types. Datasets including exome sequence, miRNA/RNA sequence, methylation, and mutation analyses for each case became publicly accessible via the TCGA Data Portal and UCSC Cancer Genomics Hub. In addition, results from cancer-specific multi-platform analyses as well as cross-cancer analyses have been published by the TCGA Network and collaborators as marker papers (see TCGA Publications website and Nature's TCGA Pan-Cancer Focus).

Recorded Lectures Meeting Agenda

Co-Chairs Carolyn Hutter, PhD Jean C. Zenklusen, PhD

# American Association

### September 2018

<u>September 2018</u>
"TCGA Legacy: Multi-Omic Studies in Cancer" Symposium held in conjunction with *Cell* from September 27-29, 2018 in Washington, DC.

#### Full Conference Program

# Meeting Overview Statement

The Cancer Genome Atlas (TCGA) has been a landmark effort to generate comprehensive, multidimensional maps of genomic changes on over 11,000 cancer cases from 33 different cancer types. This symposium will peer into the future of multi-omic studies in cancer and highlight TCGA's legacy to the field. The meeting will feature the latest advances on the genomic underpinnings of cancer, discuss the ongoing revolution in cancer classification, and showcase recent progress toward therapeutic targeting. Our aim is to bring together participants from both within and outside of the TCGA Network to stimulate exciting discussions, foster collaborations, and accelerate the translation of basic research discoveries to new cancer treatments.

# Symposium Themes

Biological Discoveries Pan Cancer Analyses Selected TCGA Project Vignettes Translational Insights

Organizers (TCGA)



Carolyn Hutter, PhD Jean C. Zenklusen, PhD

Organizers (Cell Press) Robert Kruger, MPhil, PhD Harmony Turk, PhD

# **Additional Resources**

NCI TCGA Program Website
National Human Genome Research Institute (NHGRI) TCGA Website
Official NCI website outlining the TCGA timeline and milestones

