

The National Cancer Institute: Leading Cancer Research in 2021 and Beyond

Norman E. Sharpless, M.D.

*94th Meeting of the National Advisory Council
for Human Genome Research (Virtual)*

September 13, 2021

@NCIDirector
@TheNCI

NATIONAL CANCER ACT MINISERIES

NOTHING WILL STOP US 50

Cancer innovation

2021 marks the 50th anniversary of the National Cancer Act of 1971 — legislation that intended to end the "war on cancer" by expanding funding and authorities to the National Cancer Institute. Half a century since the act was signed into law, NCI and the biomedical research community have made leaps and bounds in cancer research, clinical trials, diagnostics and treatment. As NCI and the country continue to fight the war on cancer today, GovernmentCIO Media & Research is collaborating with the institute to bring you a six-part HealthCast miniseries to commemorate the National Cancer Act's impact. We're releasing episodes every other month throughout 2021 leading to the act's official anniversary in December.



50 Years of Cancer: Progress in Overcoming Health Disparities

Making the fight against cancer more equitable requires diversifying cancer research, clinical trials and treatments.
Jun 30, 2021



50 Years of Cancer: The Road to Better Treatments and Diagnostics

Clinical trials, innovation in research, and technology have improved cancer care in public health.
Apr 29, 2021



Ned Sharpless, MD @NCIDirector · Jun 16

Looking forward to participating in a dialogue on the great progress in #CancerResearch since the #NationalCancerAct of 1971, and the next 50 years, with @CNN's Andrew Kaczynski (@KFILE) tomorrow at 11 am ET on #WashingtonPostLive. #NothingWillStopUs

CANCER HISTORY PROJECT WHERE KNOWLEDGE EXCHANGE CREATES POSITIVE CHANGE ASCO

ABOUT | ARCHIVES | LATEST ARTICLES

NCI Oral History Project Interview with Vincent T. DeVita, Jr., M.D.

Documents

Annual Plan & Budget Proposal for Fiscal Year 2023





**Clinical Trials: Bringing
Cancer Research to All
Possible Participants**



**Computer-Based Drug Design:
Advancing the Discovery of
New Cancer Medicines**

HIGHLIGHTED SCIENTIFIC OPPORTUNITIES



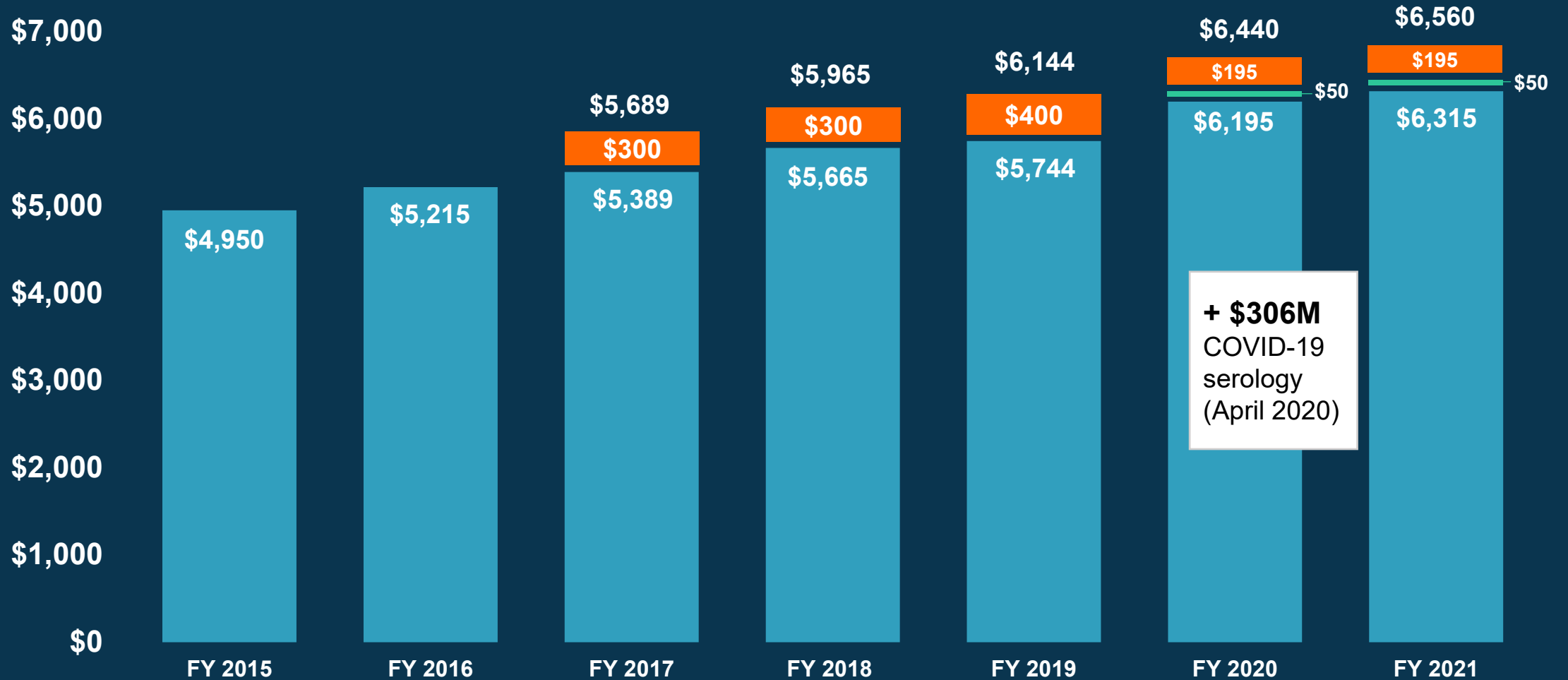
**Precision Prevention:
Predicting and
Intercepting Your Cancer**



**Tumor Dynamics:
Predicting Cancer's Trajectory
Using Tumor Atlases**

NCI Appropriations FY 2015 – 2021 (in millions)

21st Century Cures Act - orange
Childhood Cancer Initiative - green



December 13, 2005



TCGA Launch at the National Press Club

April 3, 2018



Publication of the Pan-Cancer Atlas

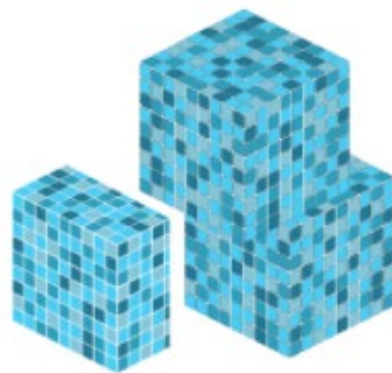
TCGA

by the numbers

TCGA produced over

2.5

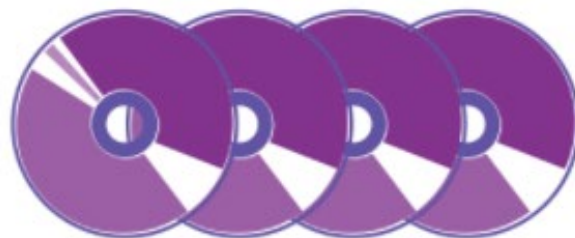
PETABYTES
of data



To put this into perspective, **1 petabyte** of data is equal to

212,000

DVDs



TCGA data describes



33

DIFFERENT
TUMOR TYPES

...including

10

RARE
CANCERS

...based on paired tumor and normal tissue sets collected from



11,000

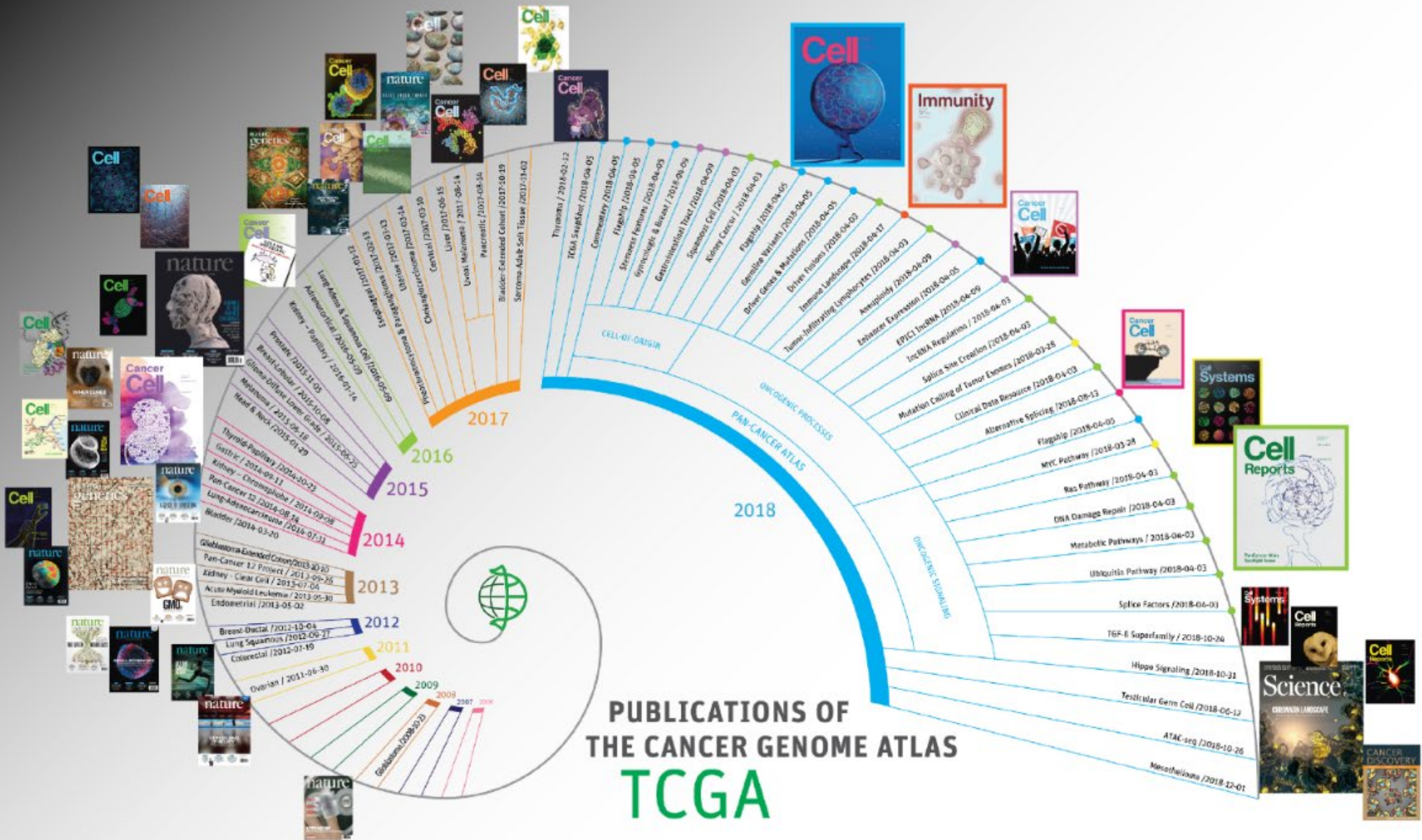
PATIENTS

...using

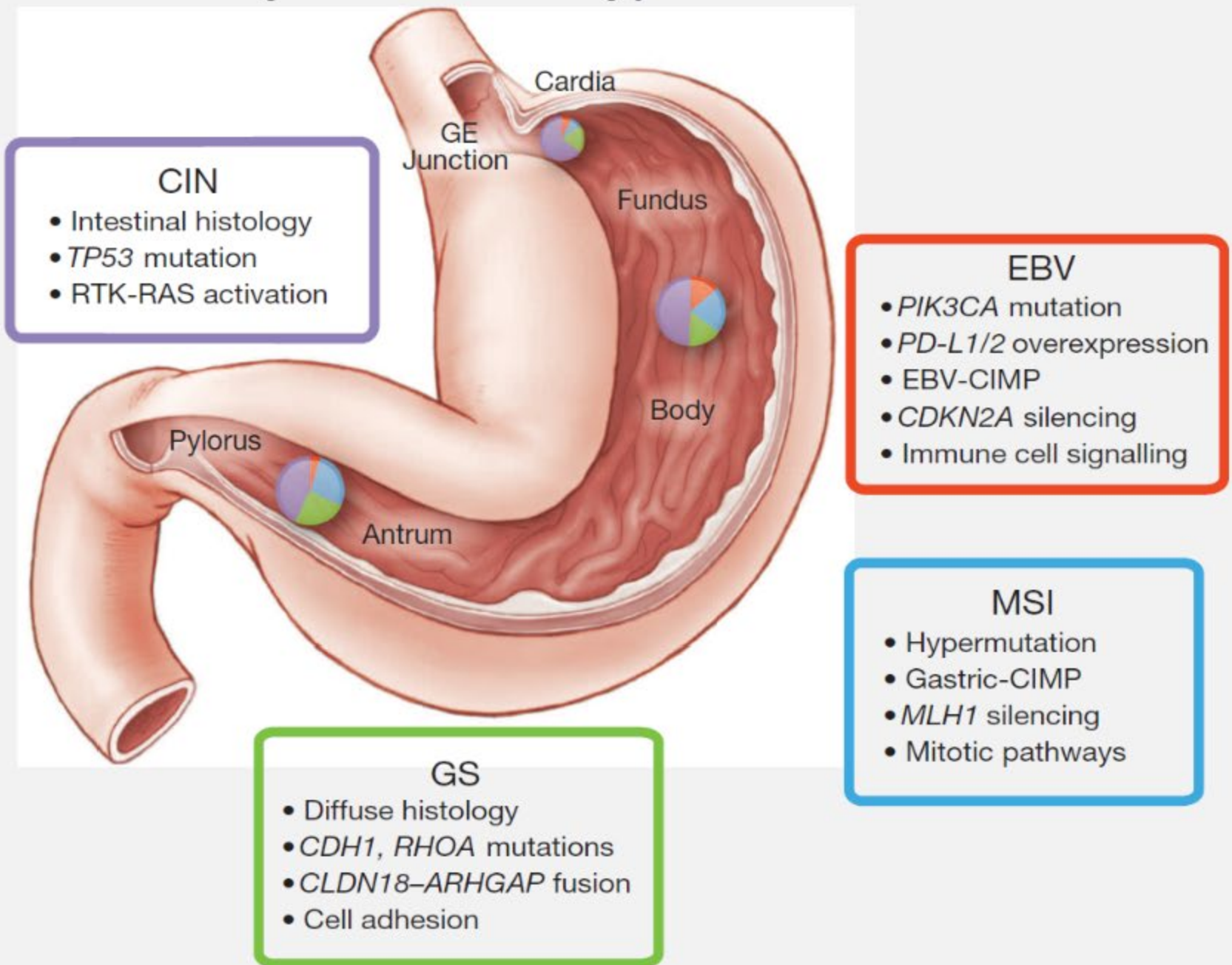
7

DIFFERENT
DATA TYPES





Four Molecularly Distinct Subtypes of Gastric Cancer



JEAN C. ZENKLUSEN, CAROLYN HUTTER and the Cancer Genome Atlas Team

2015 WINNER
PEOPLE'S CHOICE AWARD

Mapped thousands of gene sequences for more than thirty types of cancer, advancing precision medicine in the diagnosis, treatment and prevention of these deadly diseases.



Genomic Data Commons Data Portal

Harmonized Cancer Datasets

Genomic Data Commons Data Portal

Get Started by Exploring:

Projects Exploration Analysis Repository

Q e.g. BRAF, Breast, TCGA-BLCA, TCGA-A5-A0G2

Data Portal Summary [Data Release 29.0 - March 31, 2021](#)

PROJECTS

68

PRIMARY SITES

67

CASES

84,609

FILES

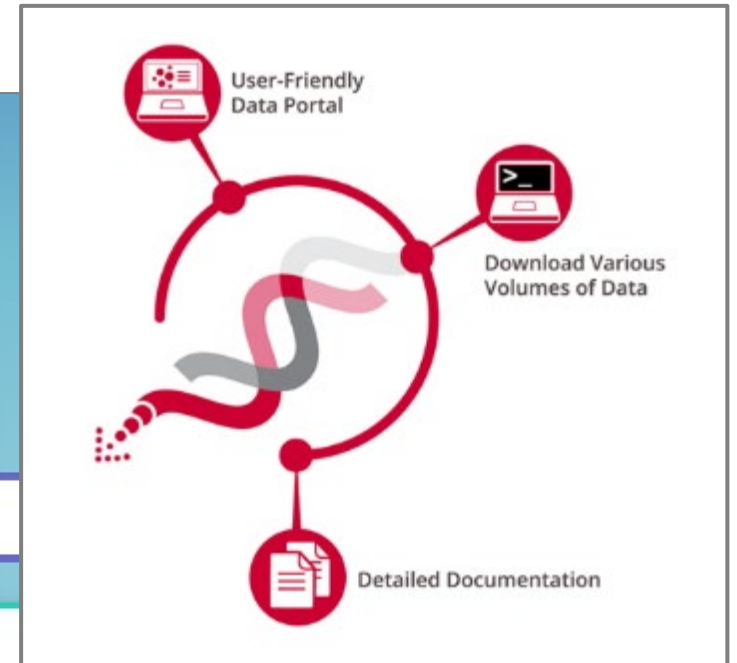
618,198

GENES

23,587

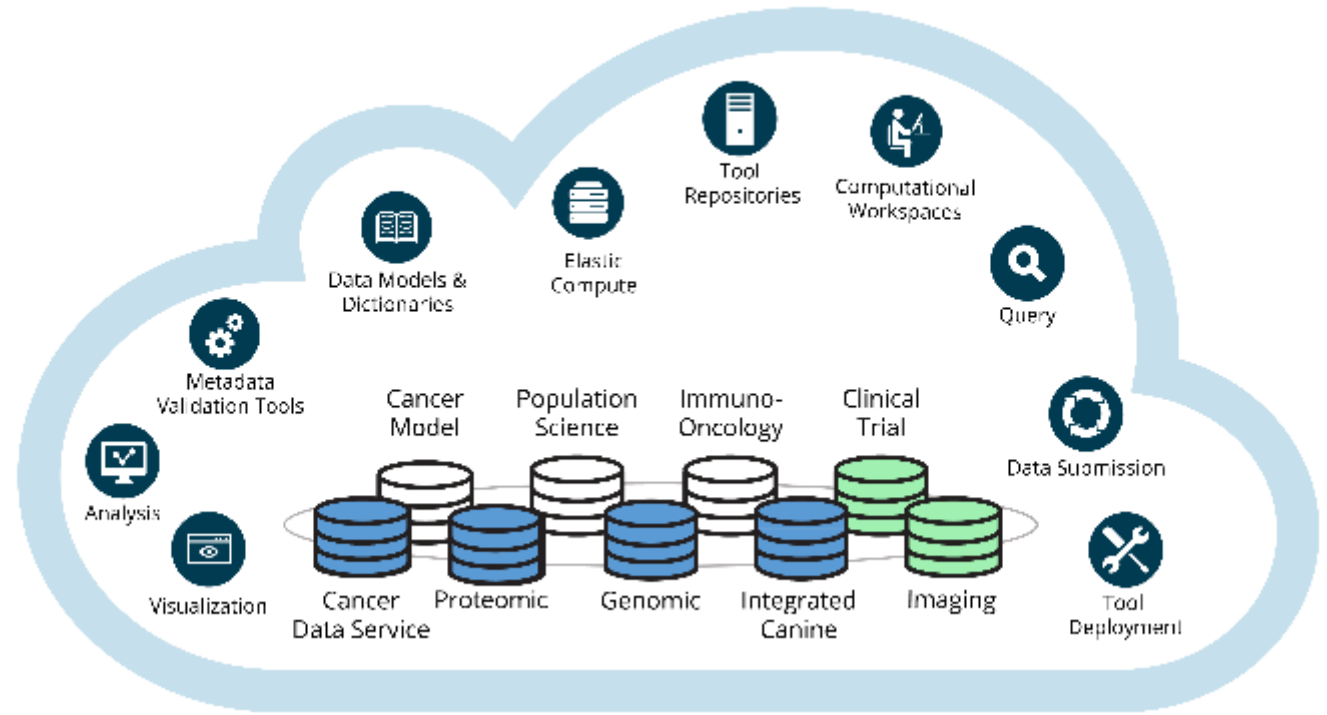
MUTATIONS

3,587,082

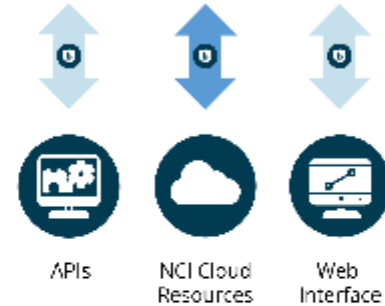


NCI Cancer Research Data Commons

Cloud-based **data science infrastructure** that provides secure access to a **large, comprehensive, and expanding** collection of cancer research data



Authentication & Authorization



Data Contributors & Consumers





Childhood Cancer Data Initiative

- 1** Gather data from every child, adolescent, and young adult diagnosed with a pediatric cancer, regardless of where they receive their care
- 2** Create a national strategy of appropriate clinical and molecular characterization to speed diagnosis and inform treatment for all types of pediatric cancers
- 3** Develop a platform and tools to bring together clinical care and research data that will improve preventive measures, treatment, quality of life, and survivorship for pediatric cancers

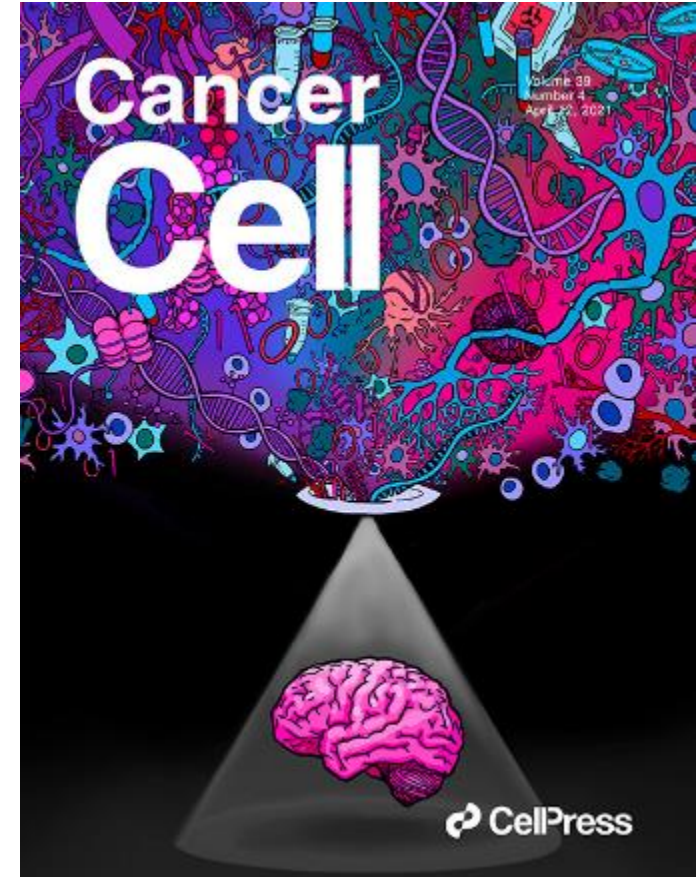
**Childhood Cancer
Data Platform**

**National Childhood
Cancer Cohort**

**Childhood
Molecular
Characterization
Protocol**

Proteogenomic and metabolomic characterization of human glioblastoma

- Phosphorylated PTPN11 and PLCG1 represent a signaling hub in RTK-altered tumors
- Four immune GBM subtypes exist, characterized by distinct immune cell populations
- Mesenchymal subtype EMT signature is specific to tumor cells, but not to stroma
- Histone H2B acetylation is enriched in classical GBMs with low macrophage content



Wang et al., 2021, *Cancer Cell* 39, 509–528
April 12, 2021 <https://doi.org/10.1016/j.ccell.2021.01.006>

SHERLOCK LUNG

Tracking Lung Cancer Mutational Processes **in Never Smokers**

232 Patients

General Population
Never Smokers
European Descent



Whole Genome Sequencing

Tumor Tissue 85x
Blood/Normal Tissue 32x



How Tumors Were Evaluated

- Genomic Landscape
- Mutational Signatures
- Evolutionary History
- Molecular Subtypes
- Clinical Outcome

SHERLOCK LUNG

Findings

Burden of Genomic Alterations Impacting Survival

● Identification of Genomic Subtypes

f

Forte (20%)

Smoker Like Features
(WGD)

mf

Mezzo-forte (30%)

EGFR Mutations

p

Piano-Adenos (34%)

Stem Cell Like Features

p

Piano-Carcinoids (14%)

Stem Cell Like Features

APOBEC Signature; SBS18

Alkylating Signatures; SBS8

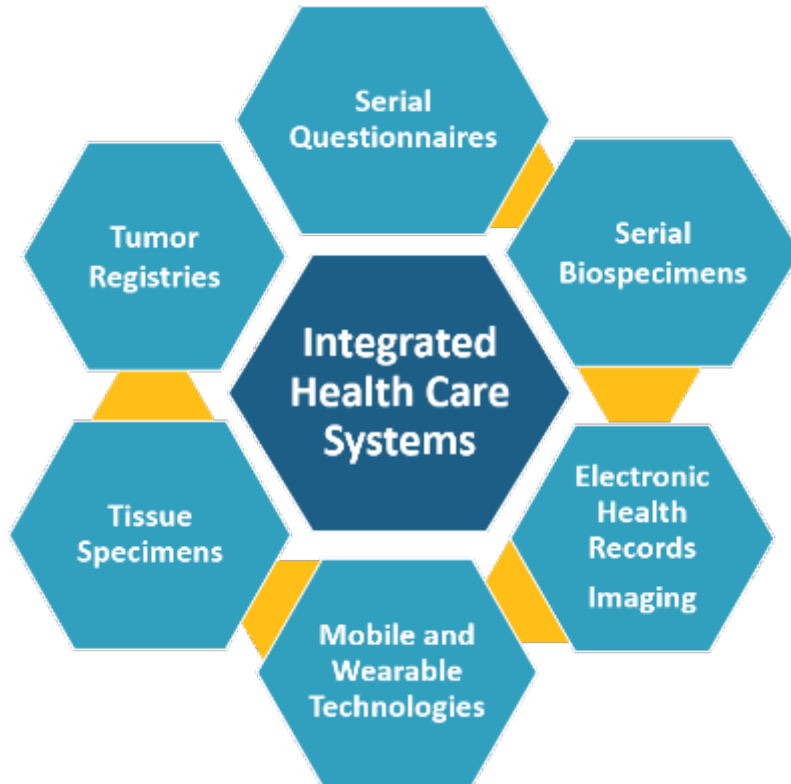
Germline *AR*; *UBA1*; *NKX2-1*

↓ Latency ↑

MYC; *HLA LOH*; *MCL1*; *RBM10*

EGFR; *UBA1*; *ERBB2*; *ARID1A*

Connect for Cancer Prevention Study



- Prospective cohort of 200,000 adults in the United States
- Designed to further investigate the etiology of cancer and its outcomes, which may inform new approaches in precision prevention and early detection
- Will capitalize on research innovations to advance the field of cancer epidemiology and prevention including:
 - New technologies for exposure assessment
 - Large-scale analyses of the genome, epigenome, transcriptome, proteome, metabolome, microbiome
 - Molecular profiling of tumors and precursor lesions



Confluence

Uncovering breast cancer genetics

>300,000
Breast
Cancer
Patients



>300,000
Controls

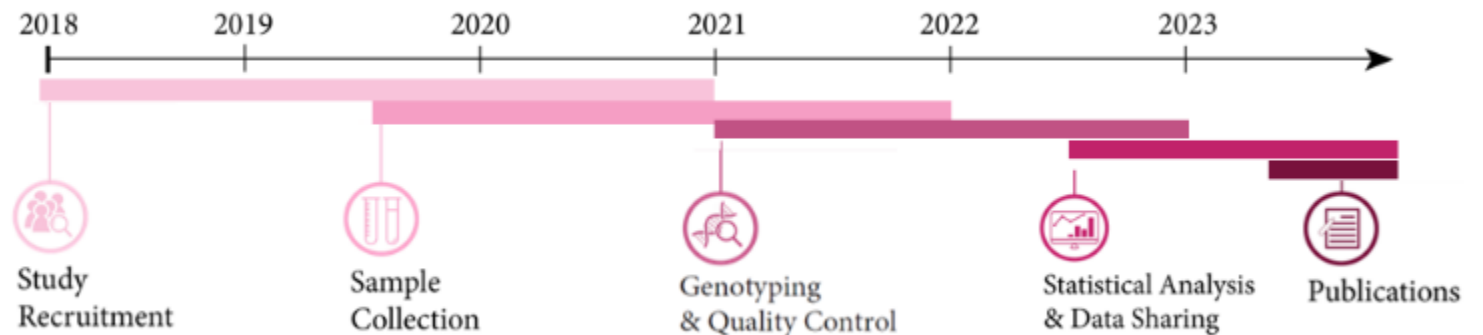


International
and multi-
ancestry



Multi-ancestry genome-wide association study (GWAS) to:

- Discover variants for breast cancer risk overall and by subtype
- Develop multi-ancestry polygenic risk scores for personalized risk assessment
- Discover variants for breast cancer survival, pharmacogenomics, and second cancers



Novel Uses of Sequencing

Mutational signatures to determine etiology



Blood-based multi-cancer early detection (MCED) tests





NCI Symposium on

MUTATION SIGNATURES AND CANCER

December 2–3, 2021

<https://events.cancer.gov/nci/mutationsignatures>

Invited Speakers:

Ludmil Alexandrov, Ph.D., University of California, San Diego

Maria Teresa Landi, M.D., Ph.D., National Cancer Institute

Peter Campbell, Ph.D., Wellcome Trust Sanger Institute

Phil Jones, M.D., Ph.D., University of Cambridge

Elli Papaemmanuil, Ph.D., Memorial Sloan Kettering

Gad Getz, Ph.D., Broad Institute

Steven Rozen, Ph.D., Duke-NUS

Allan Balmain, Ph.D., University of California, San Francisco

Serena Nik-Zainal, M.D., Ph.D., University of Cambridge

Reuben Harris, Ph.D., University of Minnesota

Adam Shlien, Ph.D., University of Toronto

Teresa Przytycka, Ph.D., National Center for Biotechnology Information

David Wedge, Ph.D., University of Manchester

Peter Park, Ph.D., Harvard University

Joshua Campbell, Ph.D., Boston University

Ludmila Prokunina-Olsson, Ph.D., National Cancer Institute

Hannah Carter, Ph.D., University of California, San Diego

Nuria Lopez-Bigas, Ph.D., IRB Barcelona

Division of Cancer Control and Population Sciences Leadership



Robert T. Croyle, Ph.D.
Director
NCI Division of Cancer Control and
Population Sciences
Retiring December 2021



Katrina Goddard, Ph.D.
Kaiser Permanente Center
for Health Research
*Incoming DCCPS Director
pending final reviews.*

Discussion