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PROJECT GENIE
Genomics Evidence Neoplasia Information Exchange

Opportunities and Lessons Learned from AACR's Project GENIE

Presented By:
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Vanderbilt University representative to the GENIE Steering Committee
and Chair of the GENIE Operations Sub-committee
10/29/2019

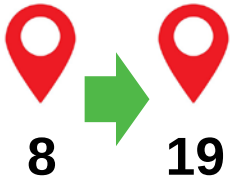
Disclosures

- **Consulting/Advisory:** GenomOncology, Personalis, Roche
- **Research funding:** Pfizer, BMS, GenomOncology
- **Equity:** GenomOncology, Personalis

GENIE Overview

- International pancancer registry built through data sharing
  - Driven by openness, transparency, and inclusion

- GOAL: improve clinical decision making
  - Linking clinical genotype to clinical outcomes



- Eight founding participants, now 19
  - North America & Europe
  - Plans for future expansion

- Sponsored research
- Collaborative projects
- Grants and philanthropy

Expanded Participants (19)

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Getting Started

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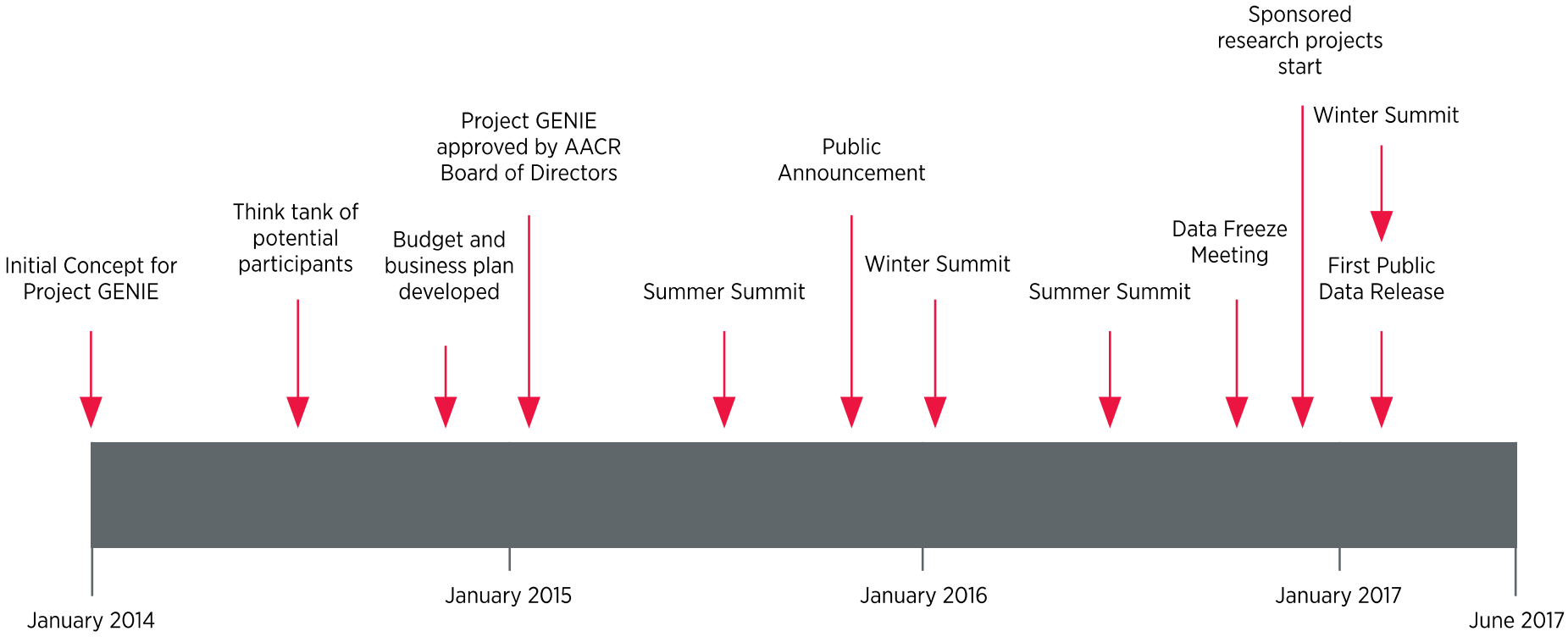


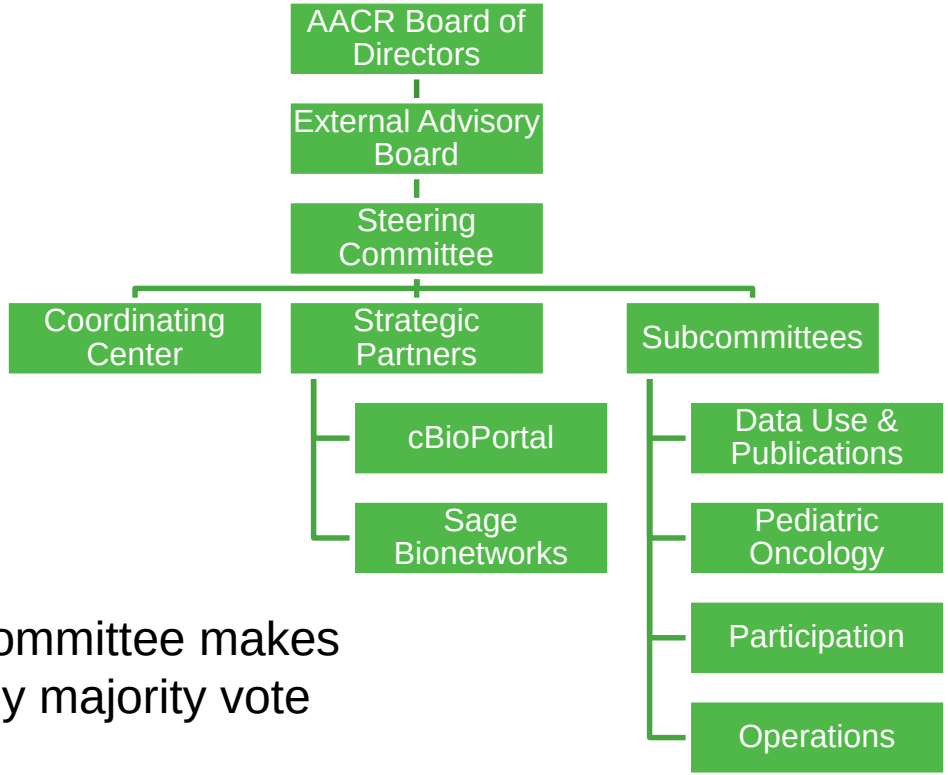
DOI: 10.1200/CCI.17.00083 JCO Clinical Cancer Informatics - published online February 16, 2018

Continued Progress

- 1st public release 1/05/2017
  - 18,860 total sequenced tumors
- 2nd release: 11/22/2017
  - 31,673 total sequenced tumors
- 3rd release: 01/09/2018
  - 39,600 total sequenced tumors
- 4th release: 07/16/2018
  - 48,500 sequenced tumors
- 5th release: 01/08/2019
  - ~60,000 sequenced tumors

GENIE will be three November 6, 2018!

Current Operating Structure



Steering Committee makes decisions by majority vote

GENIE Today

GENOMICS

✓Somatic Tumor DNA

PHENOMICS

Tumor type
Histology
Demographics
Vital status

47,500 Tumors
8 Cancer Centers

Data made publicly available 12 months after date of sequencing

Sponsored Research

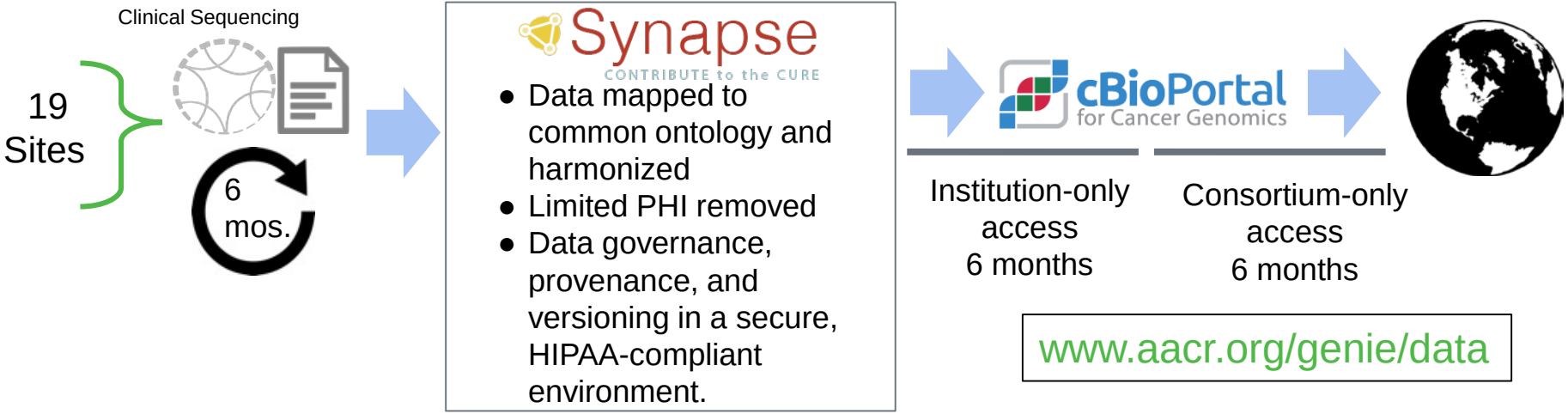
PHENOMICS

Tumor type
Histology
Demographics
Vital status
Detailed Clinicopathology
Prior Tx
Outcomes

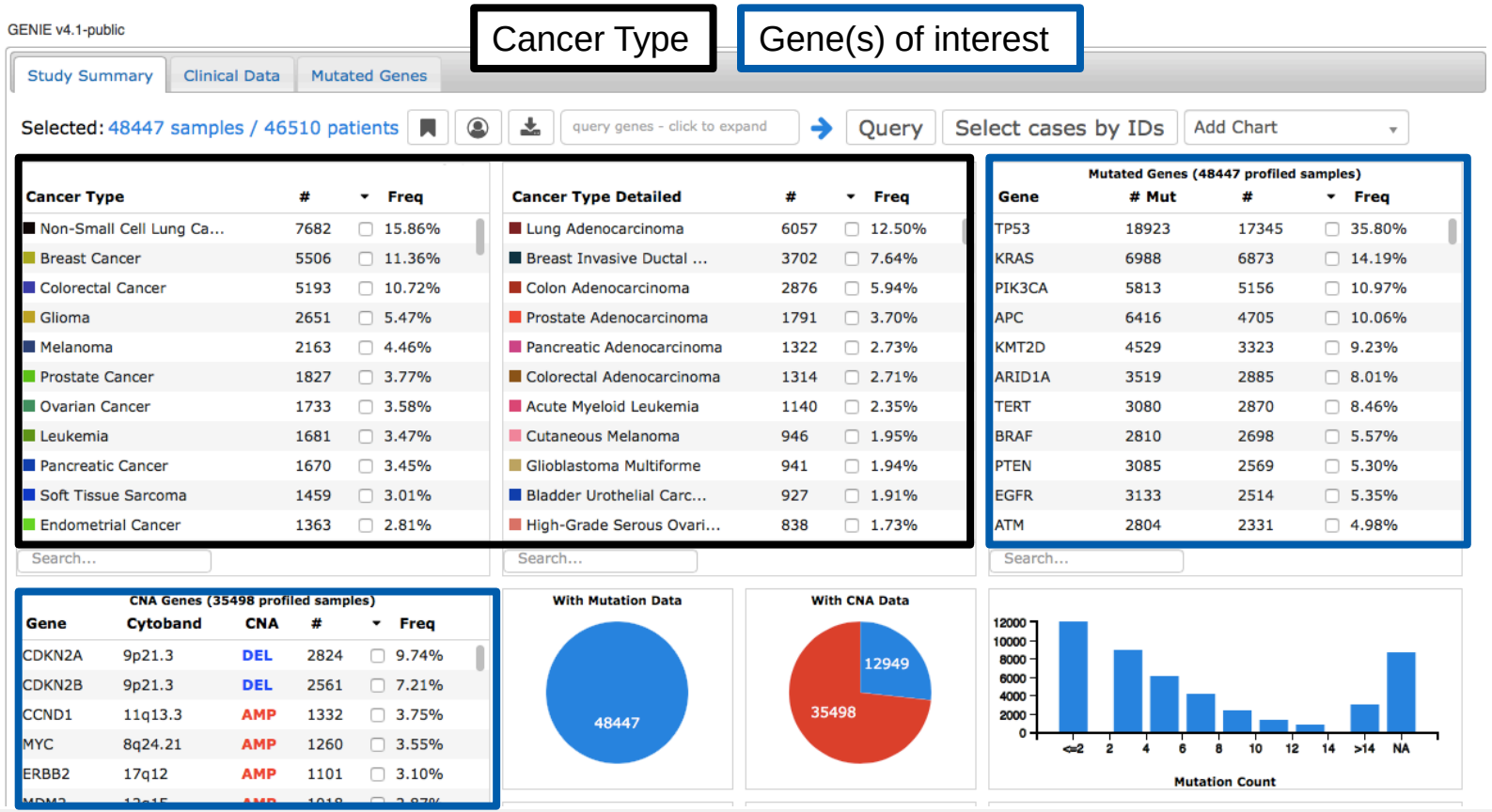
Specific Cohorts
Variable # of Centers

Data made public at time of publication

How the Registry Operates: Baseline Data

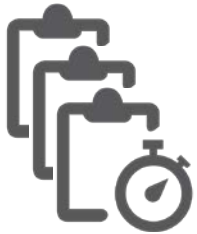


Define Virtual Cohorts of Interest



How the Registry Operates: Detailed Clinical Data

clinical queries are posed based on registry content

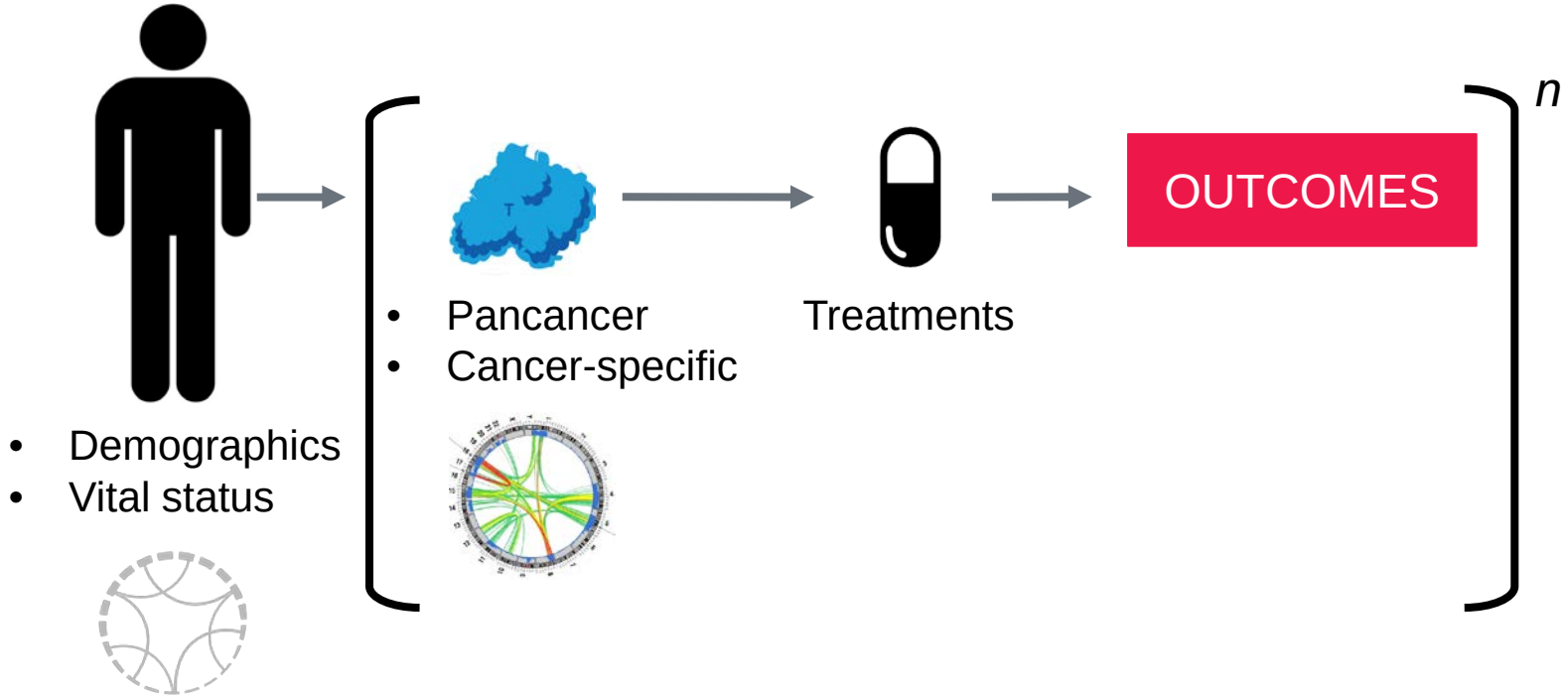


clinical data required to answer the question are manually abstracted

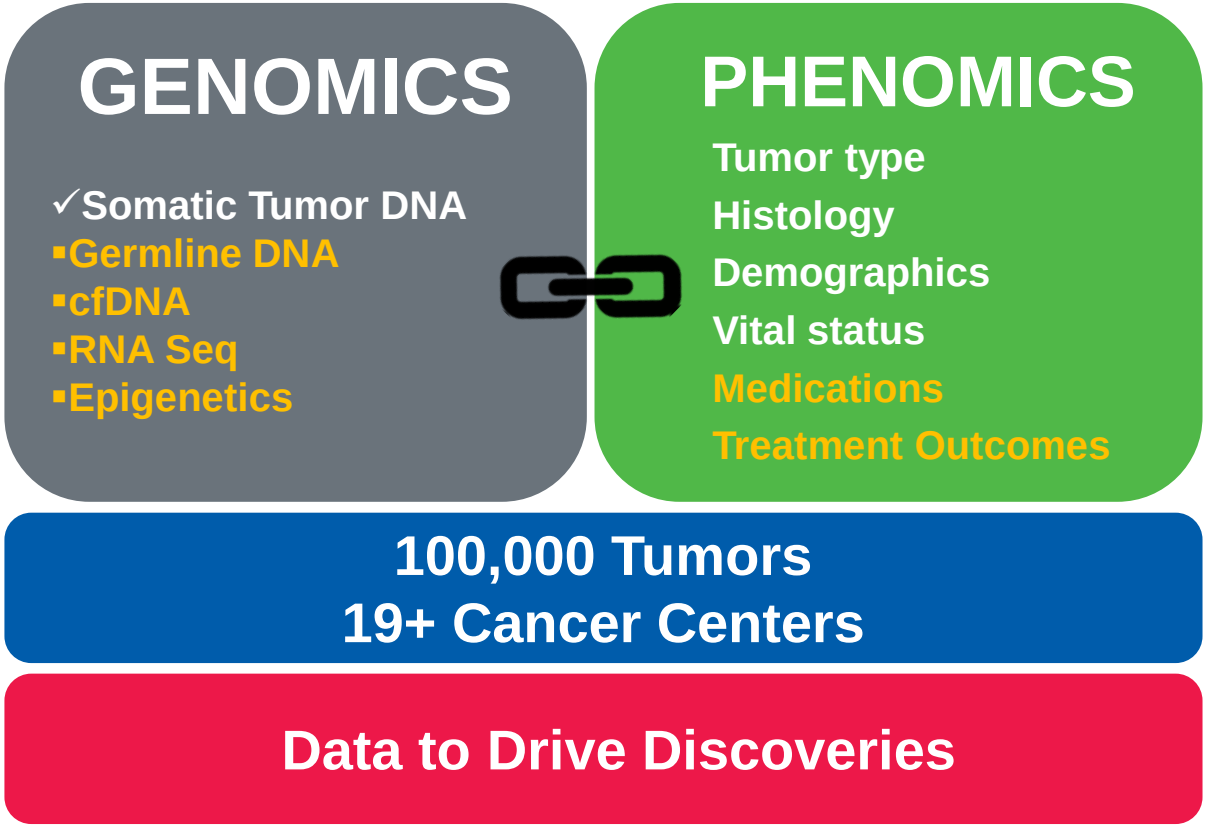
genomic and clinical data linked

Consortium/sponsor-only access to time of publication

A Cancer Patient's Journey



GENIE of Tomorrow (2.0)



Diverse Gene Panels

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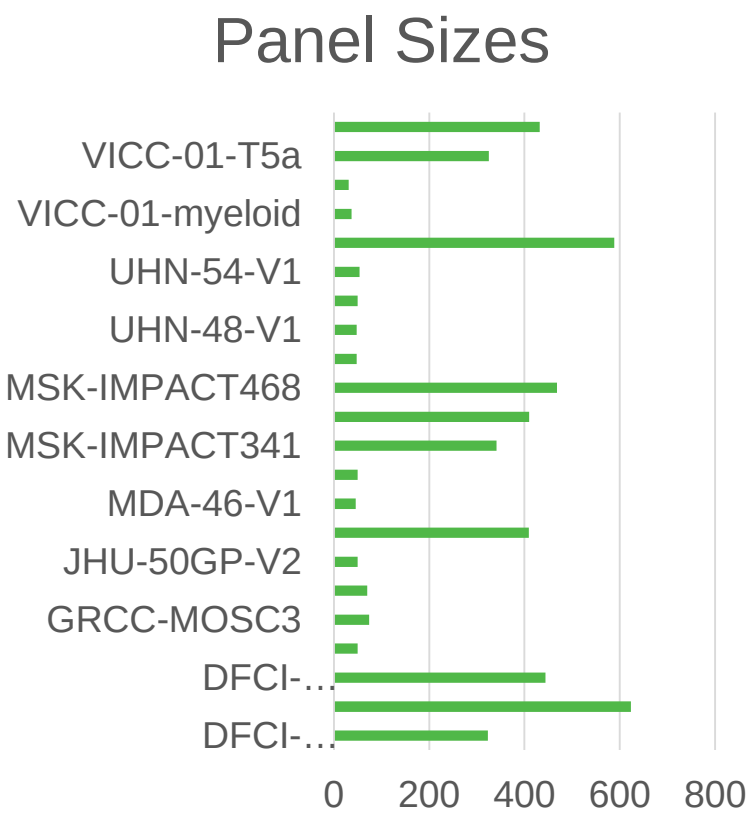

Total Genes Covered	1324
Shared by All Panels	8
Shared by All Large Panels	143

Genes Shared by All Panels

BRAF
HRAS
IDH1
KIT
KRAS
NRAS
PTEN
TP53

Shared by All Large and Solid Tumor Panels

BRAF	AKT1
HRAS	ALK
IDH1	CTNNB1
KIT	EGFR
KRAS	ERBB2
NRAS	FGFR1
PTEN	FGFR2
TP53	FGFR3
PDGFRA	MET
PIK3CA	RET

Distribution of Samples Across Centers

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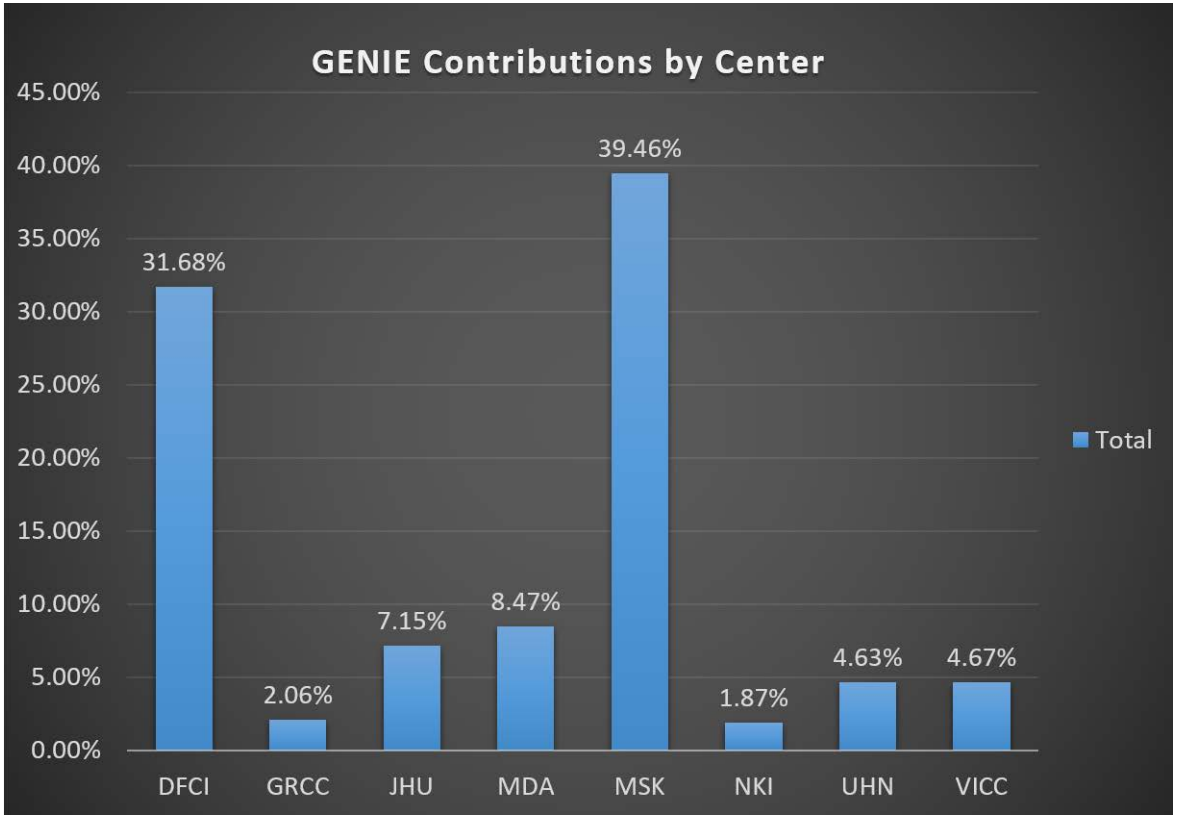

Racial and Gender Distribution

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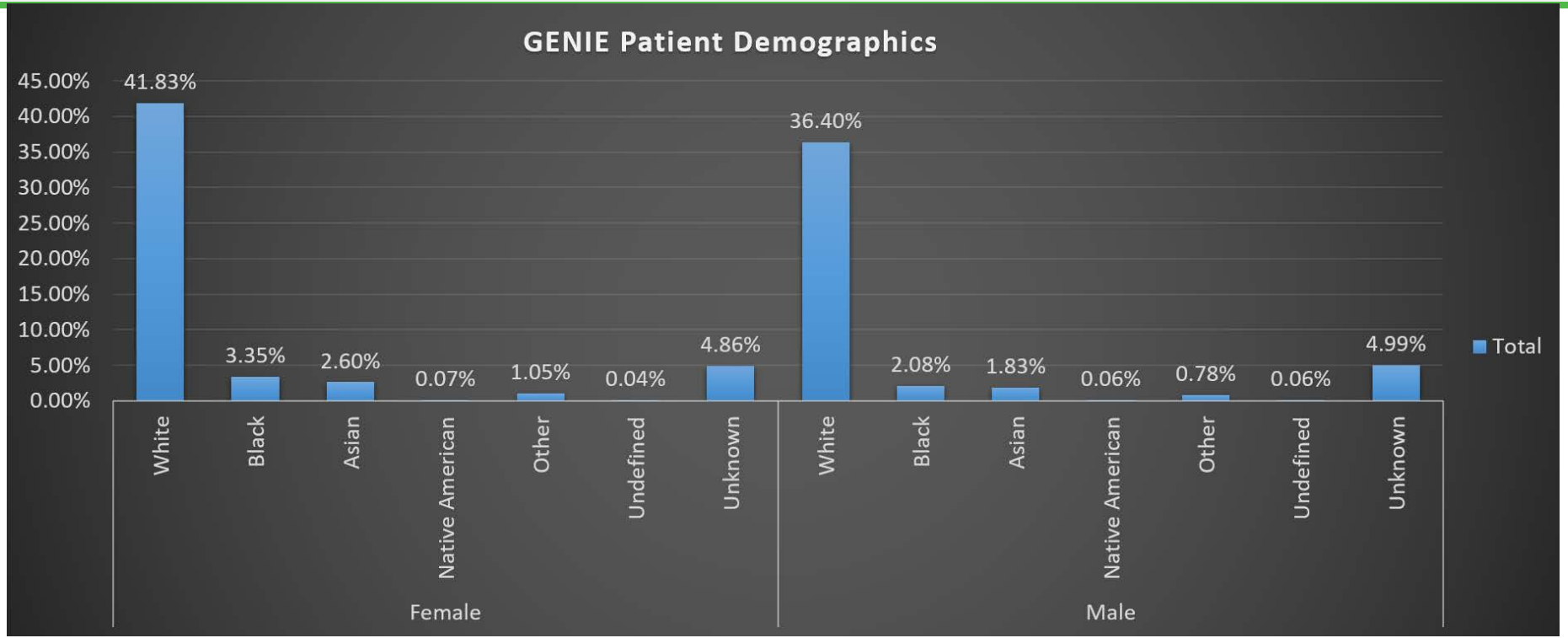

Racial Distribution by Center

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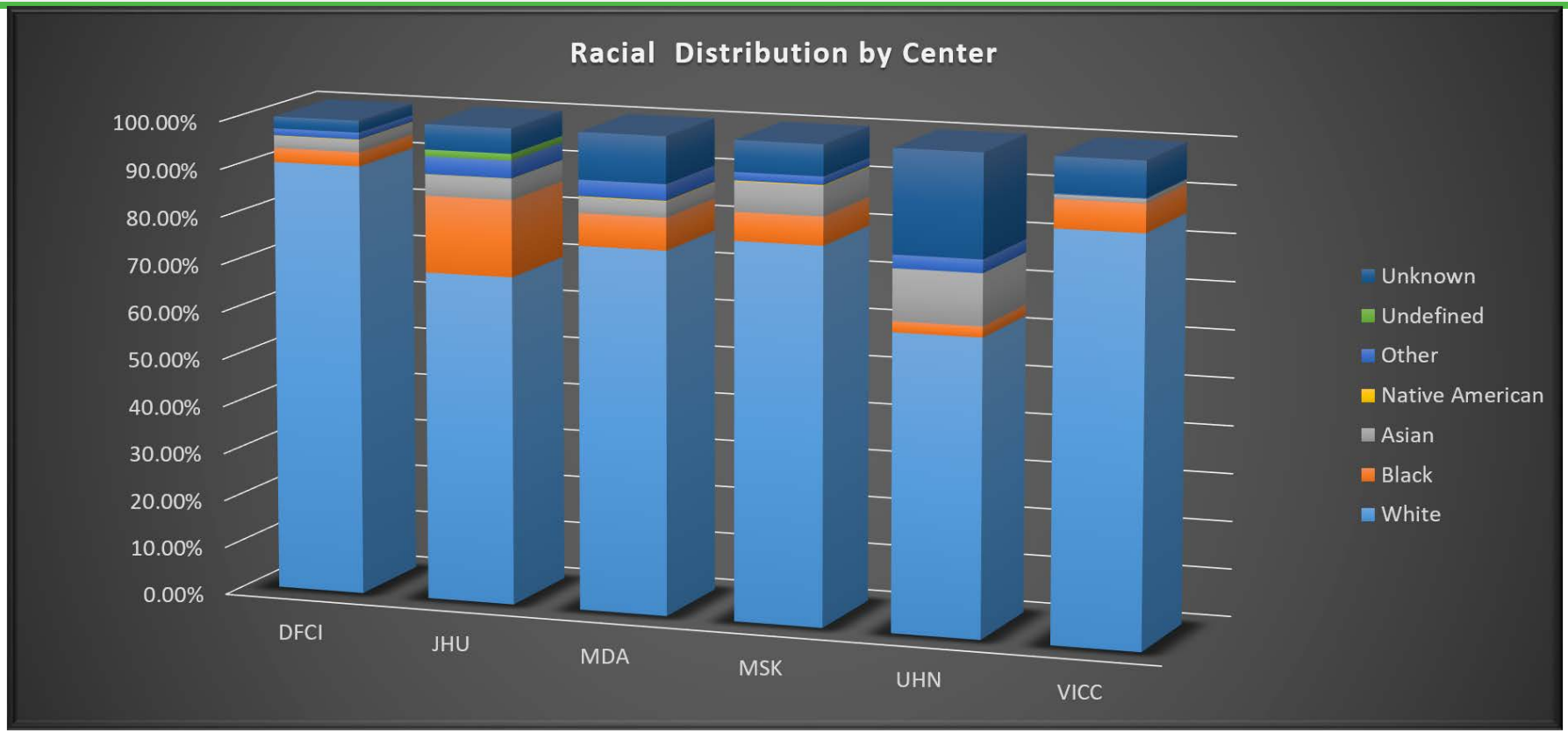

Distribution by Patient Age at Sequencing

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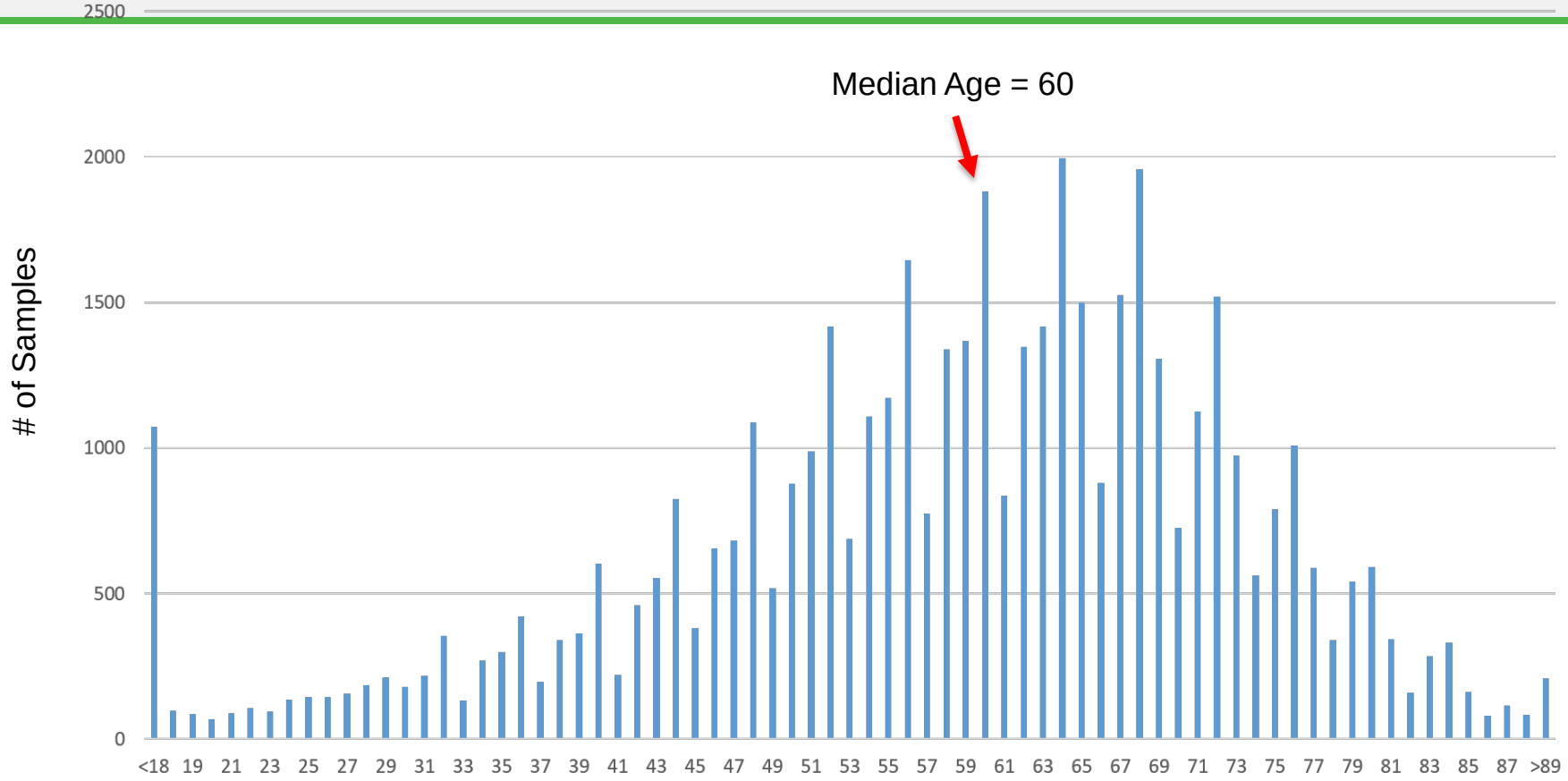

Distribution of Samples by Cancer Type

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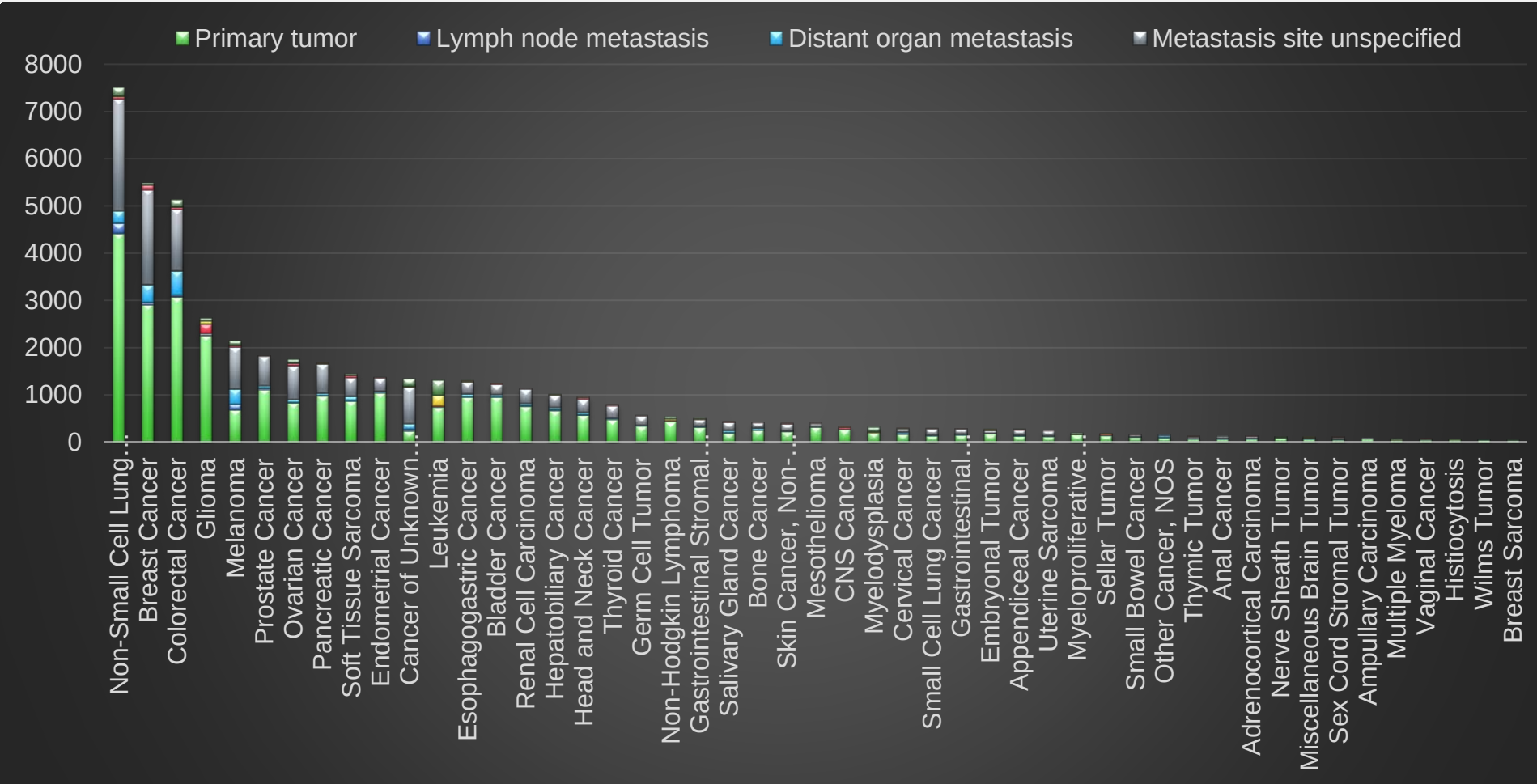

Top Mutated Genes

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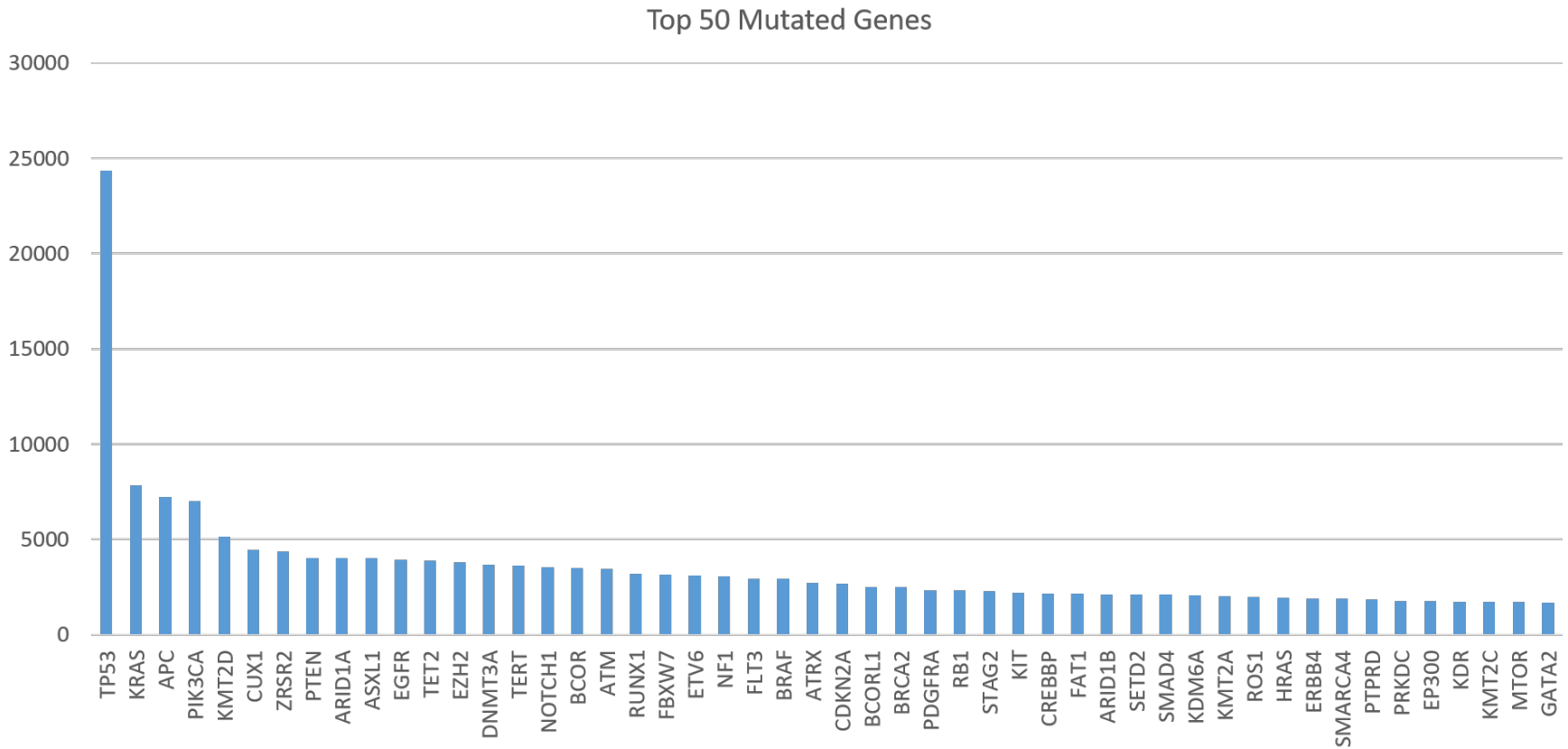
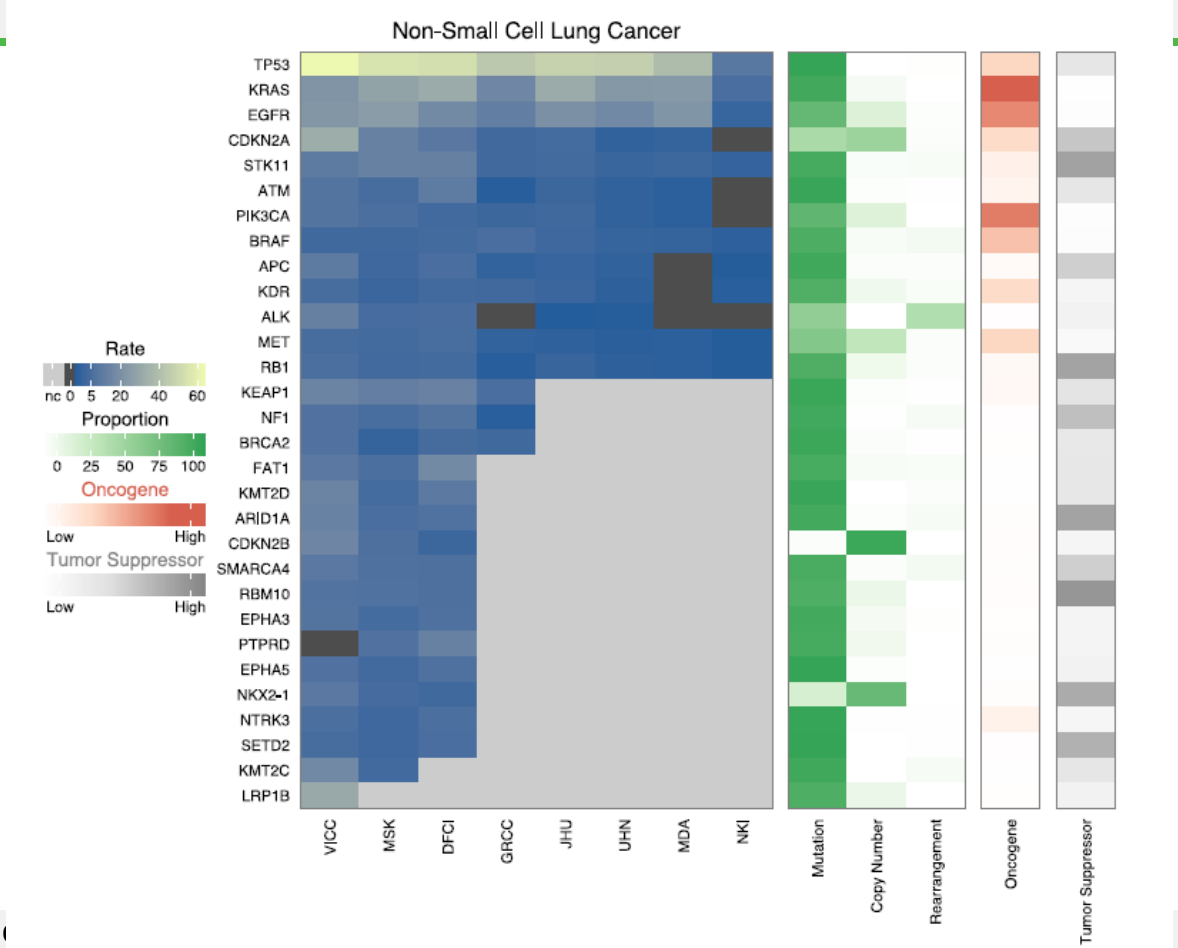


Genomic Alterations in NSCLC



AACR Project GENIE: Powering Precision Medicine through an International Consortium
The AACR Project GENIE Consortium
Cancer Discov August 1 2017 (7) (8) 818-831; **DOI:** 10.1158/2159-8290.CD-17-0151

Landscape of Clinical Actionability

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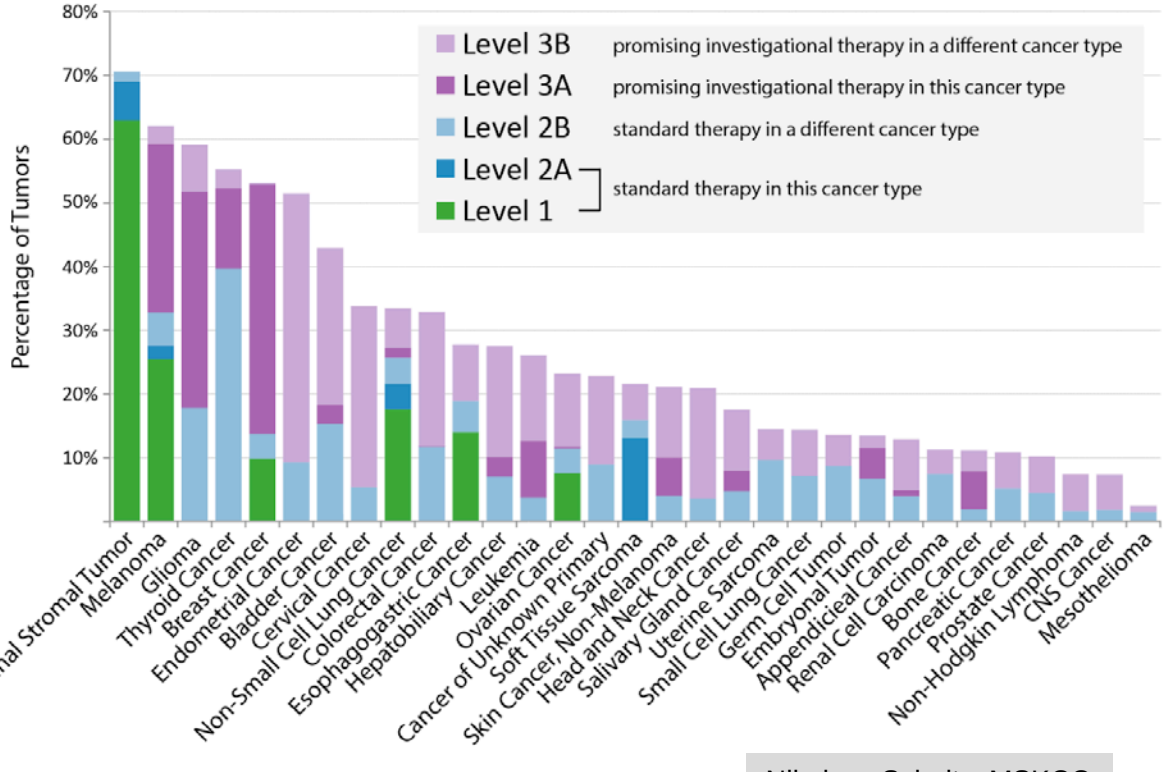

Nikolaus Schultz, MSKCC

“Actionable” Clinical Trials

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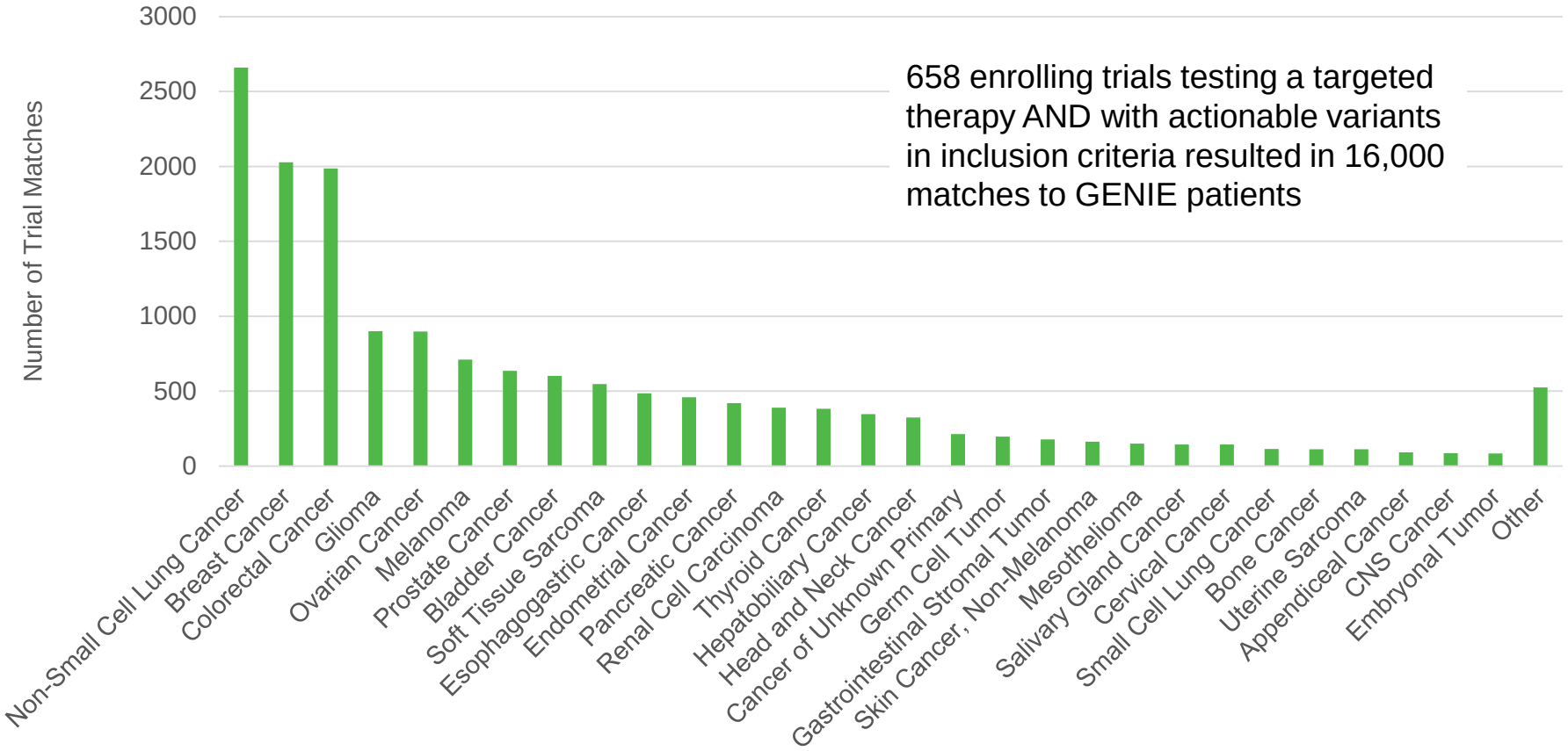

NCI-MATCH (release 3 data)

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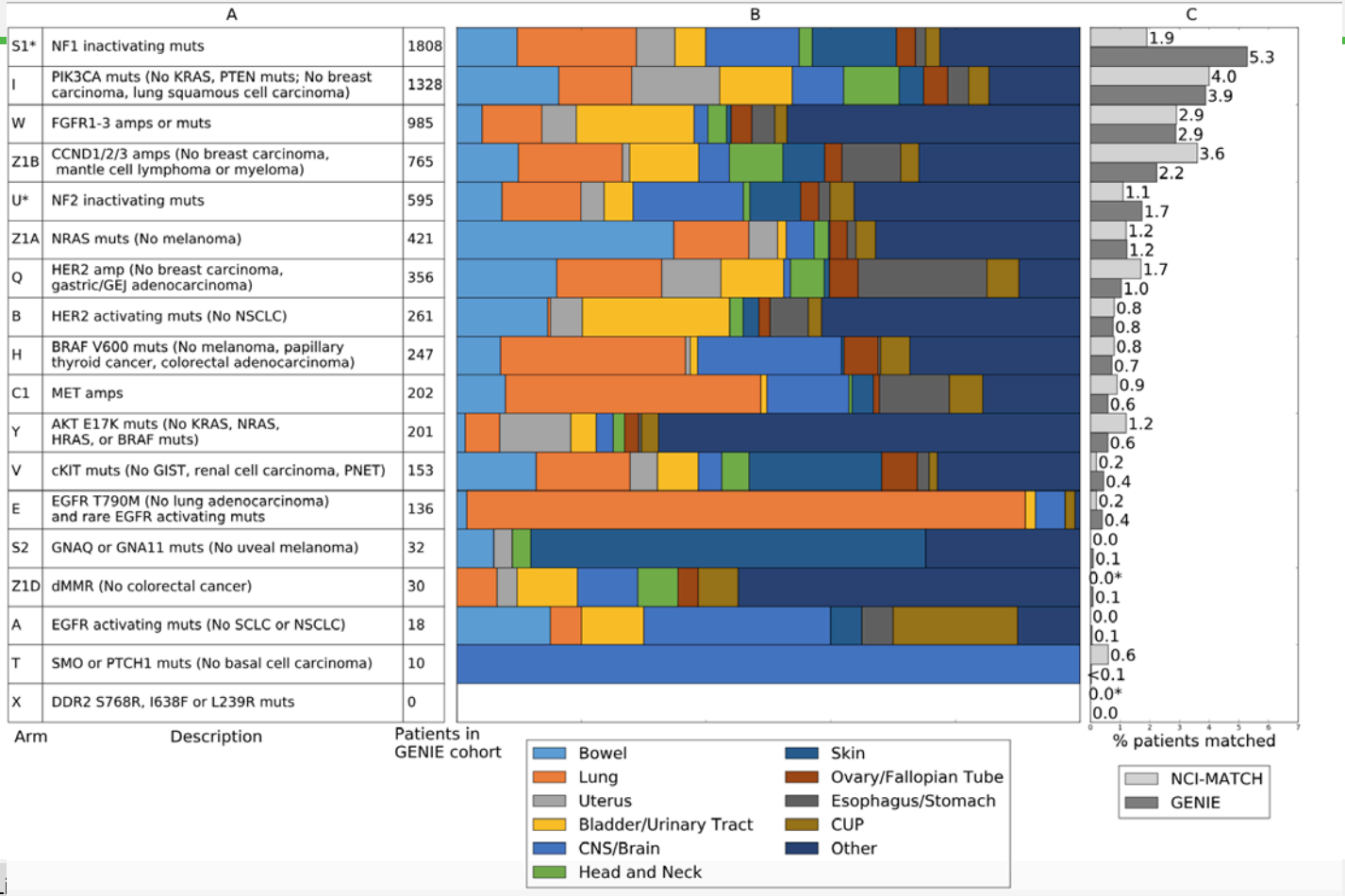


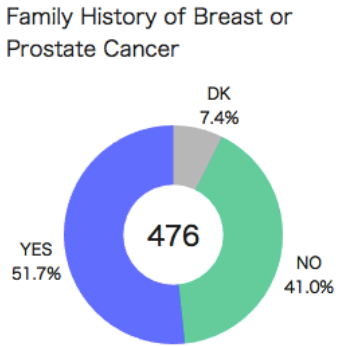
Challenges with Real-World Data

- Missing treatment information pre- and post- treatment at sequencing institution
- Missing diagnostic information, especially biomarker assessments
- Lack of information on responses to therapy
- Lack of information on reasons for discontinuation of therapy
- “Fuzzy” dates
- Resource intensive effort to gather data from outside medical records
- Limited ability of some institutions to release information for patients on clinical trials
- Relatively high proportion of patients lost to follow-up

Many Are Looking at Different Parts of the Same Problem

Patient-driven initiatives

mpcproject.org



- Count Me In (Broad Institute)
  - Metastatic Breast Cancer Project
  - Angiosarcoma Project
  - Metastatic Prostate Cancer Project
  - …
- Make an IMPACT (MSKCC)
- Similar efforts emerging
- Thousands of patients joining to share clinical and molecular data to advance research

Conclusions

- Patient as aggregator/donor of data
  - Regulation/Policy to make easier for patient to access, download, transfer their data
  - Patient “rights” to use data “What is it you know about me?”
- Funding agencies should require data deposition and require that portion of funding is used for work required to clean and deposit data
- Insufficient infrastructure for public deposition (storage, upload, download, data use)
- More publicly accessible training data for machine learning community
- Data Authorship (credit for secondary use of deposited data)
- Caution FDA to not inadvertently restrict data coming from assays

Thank you

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