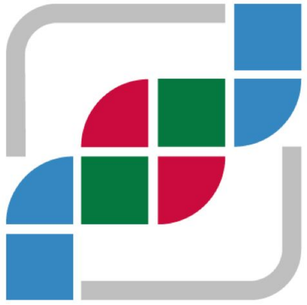


cBioPortal for Cancer Genomics

Webinar 2: Mutation Details & Patient View

May 7, 2020

Dana-Farber Cancer Institute

Memorial Sloan Kettering Cancer Center

thehyve

The Children's Hospital of Philadelphia

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

Webinar Schedule

- April 30: Introduction to cBioPortal
- May 7: Mutation Details & Patient View
- May 14: OQL & Expression
- May 21: Group Comparison
- May 28: API & R Client

All webinars are on Thursdays 11am-12pm EDT

Acknowledgements

cBioPortal for Cancer Genomics

Memorial Sloan Kettering Cancer Center

Nikolaus Schultz
Jianjiong Gao
Benjamin Gross
S. Onur Sumer
Yichao Sun
Hongxin Zhang
Adam Abeshouse
Ritika Kundra
Ino de Bruijn
Robert Sheridan
Angelica Ochoa
Aaron Lisman
Manda Wilson
Avery Wang
Jing Su
Ramyasree Madupuri
Gaofei Zhao
Xiang Li

Dana-Farber Cancer Institute

Ethan Cerami
Chris Sander
Tali Mazor
Luke Sikina
Pieter Lukasse
Priti Kumari
Augustin Luna
James Lindsay

The Children's Hospital of Philadelphia

Adam Resnick
Allison Heath
Karthik Kalletla
John Maris

Weill Cornell Medicine

Olivier Elemento
Alexandros Sigaras

thehyve

Fedde Schaeffer
Oleguer Plantalech
Pim van Nierop
Paul van Dijk
Sander Rodenburg
Sjoerd van Hagen
Kees van Bochove

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

Trevor Pugh
Kelsey Zhu

Bilkent University

Ugur Dogrusoz
Ziya Erkoc

Alumni

B. Arman Aksoy
Istemi Bahceci
Caitlin Byrne
Hsiao-Wei Chen
Ersin Ciftci
Fred Criscuolo
Leonard Dervishi
Gideon Dresdner
Andy Dufilie
Catherine Del Vecchio Fitz
Arthur Goldberg
Zachary Heins
Michael Heuer
Anders Jacobsen
Ngoc Nguyen
Erik Larsson
Dong Li
Tamba Monrose
Peter Kok
Irina Pulyakhina
Pichai Raman
M. Furkan Sahin
Kaan Sancak
Sander de Ridder
Sander Tan
Jiaojiao Wang
Stuart Watt
James Xu
Dionne Zaal
Riza Nugraha

open source

Funding: Present & past

NIH National Cancer Institute
ITCR
NCI Cancer Moonshot Human Tumor Atlas Network
AACR American Association for Cancer Research
Prostate Cancer Foundation Curing Together.
Movember Foundation
Kravis Center for Molecular Oncology
Dana-Farber Cancer Institute
Robertson Foundation
TCGA
NRNB
S2C
Starr Cancer Consortium
BCRF Breast Cancer Research Foundation
IVY Foundation — The Ben and Catherine
POETIC

Email: cbioportal@googlegroups.com @cBioPortal github.com/cBioPortal

Questions?

- Please ask questions using the Q&A feature
- We will try to answer some live, some directly, and some on future webinars
- The recording of all webinars will be posted on https://cbioportal.org/tutorials/
- If you still have questions after the webinar, please ask them via our Google Group

cBioPortal overview

- Platform for **exploratory and interactive visualization, analysis and download** of large-scale cancer genomics data sets

- **Open source** software jointly developed by Dana-Farber Cancer Institute, Memorial Sloan Kettering Cancer Center, Princess Margaret Cancer Centre, Children's Hospital of Philadelphia, and The Hyve

- **Public website** (cBioPortal.org) with public data (TCGA, ICGC, published sequencing studies)
    - Private instances are installed at academic and commercial institutions world-wide
    - You can make OncoPrints and Lollipop plots with your own data ("Visualize Your Data" page)

Answers to FAQs from first webinar

- We do not reanalyze / reprocess original data

- Variants are all mapped to the same isoforms from their genomic coordinates

- Only data available with the original publications will be available in cBioPortal
  - Mutations
  - Clinical data (often limited, sometimes more complex, incl. survival)
  - Copy-number alterations
  - mRNA expression
  - DNA methylation
  - Protein and phosphoprotein levels

Answers to FAQs from first webinar

- Use of normal samples
  - normal blood or adjacent tissue is used in mutation and copy-number analysis (study-specific, some studies don’t use matched normals)
  - display of normal mRNA expression levels is currently not supported
  - z-scores for mRNA expression are usually computed using all tumor samples as the reference pool

What data is in cBioPortal?

Data sources

PubMed

NIH THE CANCER GENOME ATLAS
National Cancer Institute
National Human Genome Research Institute

International Cancer Genome Consortium

Count Me In

CCLE Cancer Cell Line Encyclopedia

AACR American Association for Cancer Research
FINDING CURES TOGETHER™

PROJECT GENIE
Genomics Evidence Neoplasia Information Exchange

https://genie.cbioportal.org/

Background biological data
(e.g. networks, 3D protein structure)

cBioPortal for Cancer Genomics

Clinical data:

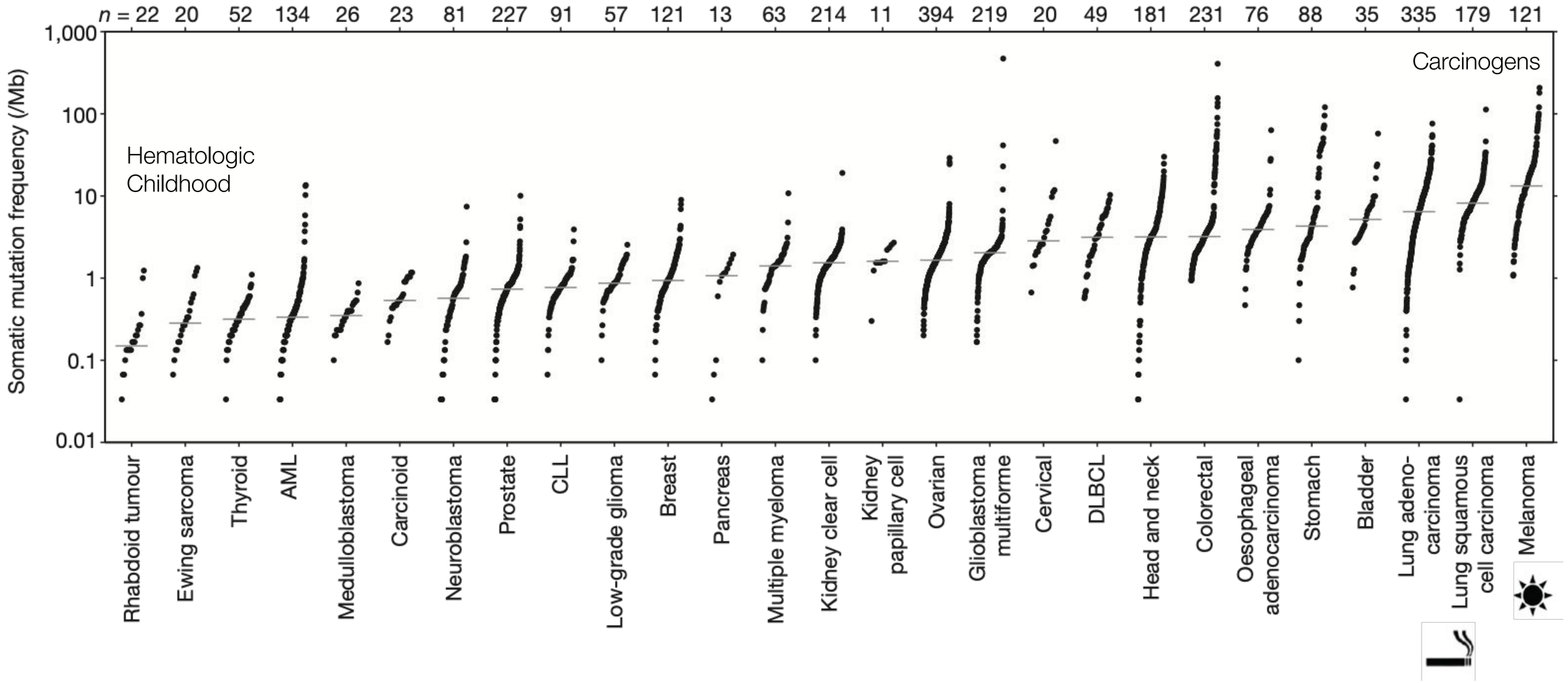
- Treatments
- Survival
- etc

Molecular data:

- Mutations
- Fusions
- Copy number
- mRNA expression
- Protein levels
- DNA Methylation*

Interpretation???

Driver vs passenger mutations - which one is which?



Lawrence MS et al., Nature, 2013

How can you distinguish drivers from VUS in cBioPortal?

cBioPortal for Cancer Genomics

Data sources

PubMed

NIH THE CANCER GENOME ATLAS
National Cancer Institute
National Human Genome Research Institute

International Cancer Genome Consortium

Count Me In

CCLE Cancer Cell Line Encyclopedia

AACR American Association for Cancer Research — FINDING CURES TOGETHER™

PROJECT GENIE
Genomics Evidence Neoplasia Information Exchange

https://genie.cbioportal.org/

Background biological data
(e.g. networks, 3D protein structure)

cBioPortal for Cancer Genomics

Curated effect & therapy implications

OncoKB
Precision Oncology Knowledge Base

CIViC
Clinical Interpretations of Variants in Cancer

My Cancer Genome®
Genetically Informed Cancer Medicine

Predicted functional effect

MA mutationassessor.org
functional impact of protein mutations

PolyPhen-2

SIFT

Variant recurrence

COSMIC
Catalogue of somatic mutations

Cancer Hotspots

Interpretation

Clinical data:

- Treatments
- Survival
- etc.

Molecular data:

- Mutations
- Fusions
- Copy number
- mRNA expression
- Protein levels
- DNA Methylation

Mutation details page: Example ERBB2

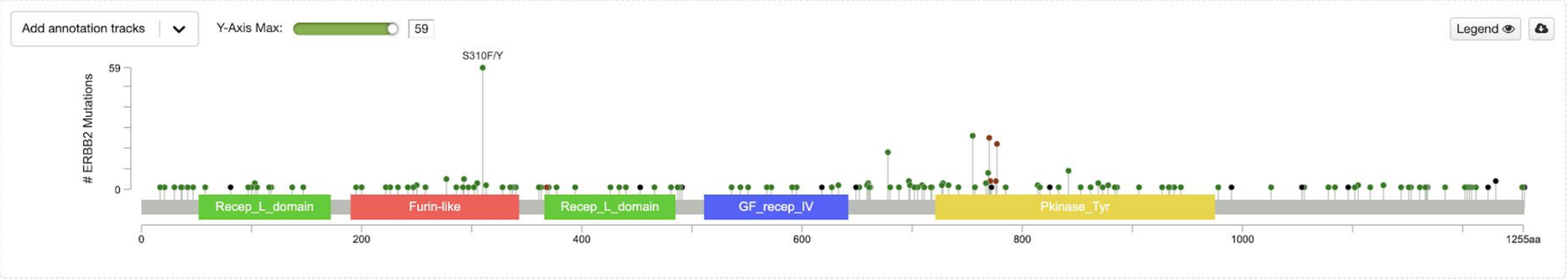
Modify Query

MSK-IMPACT Clinical Sequencing Cohort (MSKCC, Nat Med 2017)
Samples with mutation and CNA data (10336 patients / 10945 samples) - ERBB2

Queried gene is altered in • 692 (7%) of queried patients
• 726 (7%) of queried samples

OncoPrint | Cancer Types Summary | Plots | Mutations | Comparison | Survival | CN Segments | Pathways | Download

ERBB2



ERBB2

RefSeq: NM_004448
Ensembl: ENST00000269571
CCDS: CCDS32642
UniProt: ERBB2_HUMAN

Somatic Mutation Frequency 3.0%

293 Missense | 18 Truncating
52 Inframe | 10 Other

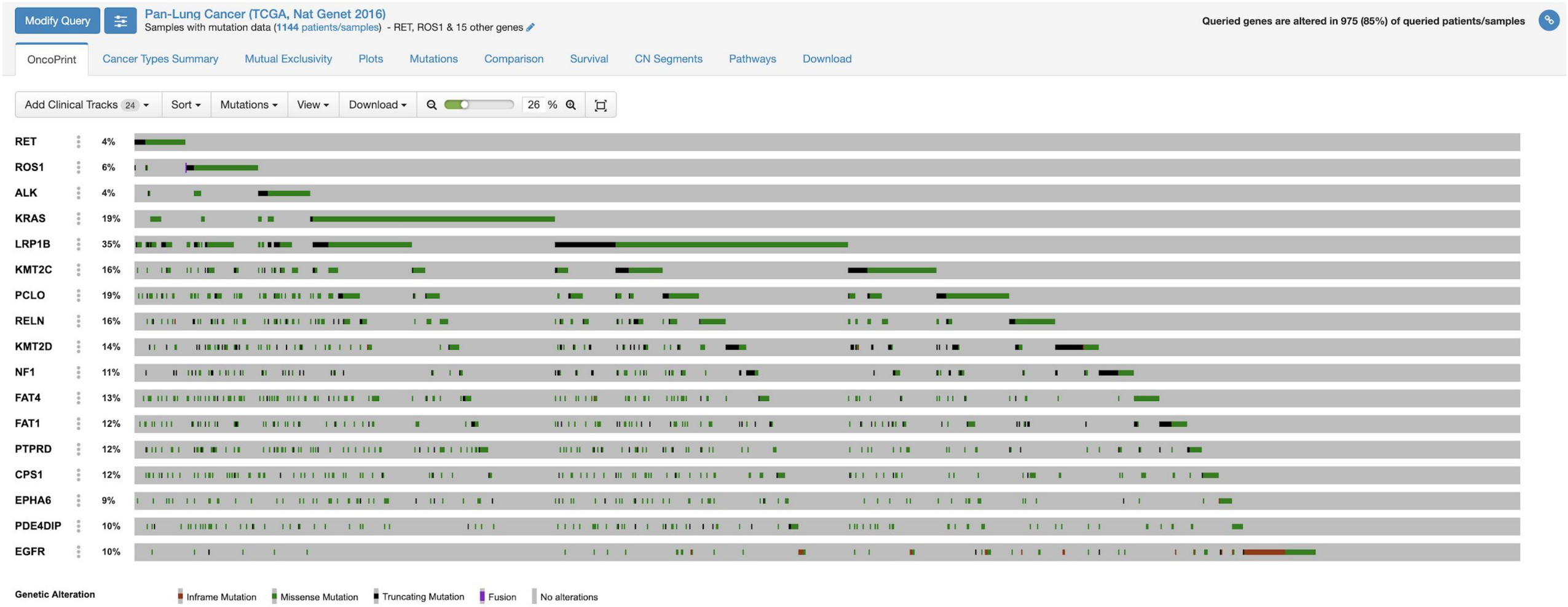
View 3D Structure

373 Mutations: includes 17 duplicate mutations in patients with multiple samples (page 1 of 15)

Columns

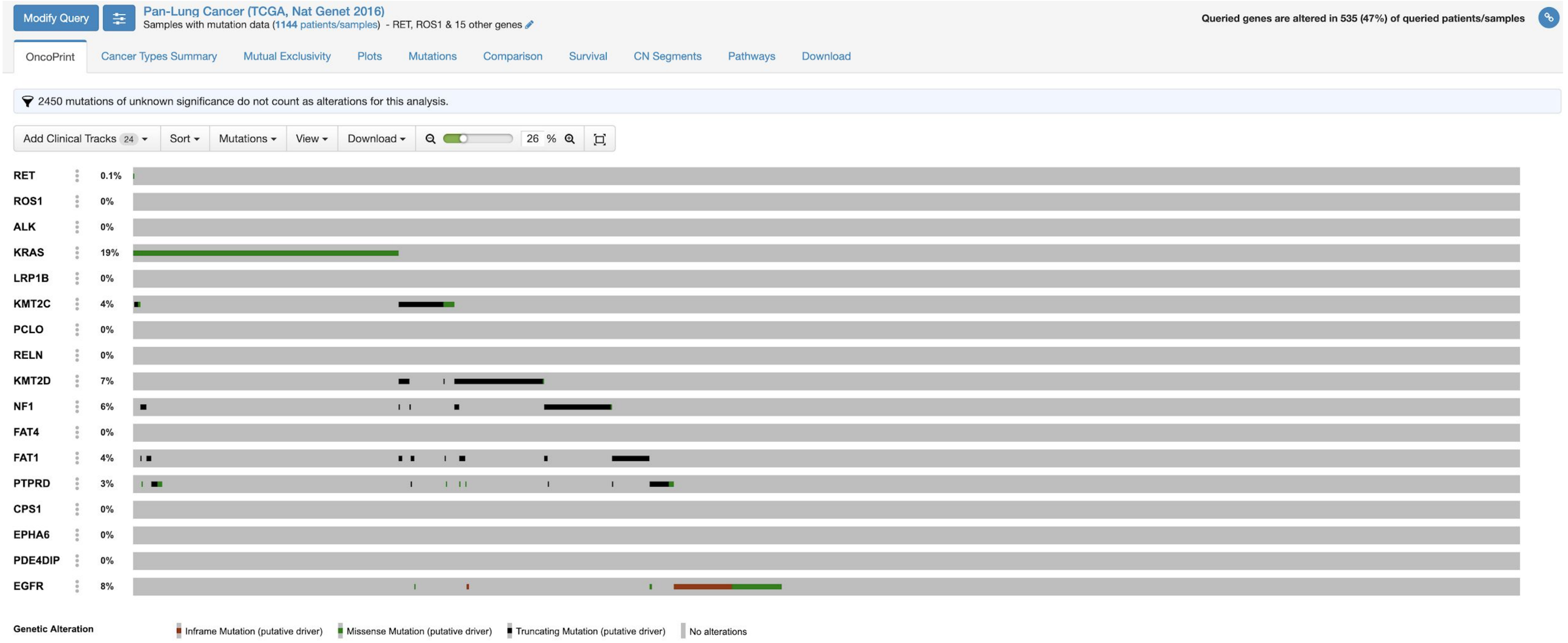
Sample ID	Cancer Type	Protein Change	Annotation ▼	Mutation Type	Copy #	COSMIC	Allele Freq (T)	# Mut in Sample
P-0009555-T01-IM5	Lung Adenocarcinoma	*L755P*		Missense	Diploid	35	0.07	1
P-0010300-T01-IM5	Lung Adenocarcinoma	*L755P*		Missense	Amp	35	0.43	4
P-0010927-T01-IM5	Lung Adenocarcinoma	*L755P*		Missense	Diploid	35	0.34	5
P-0010927-T02-IM5	Lung Adenocarcinoma	*L755P*		Missense	Diploid	35	0.26	3
P-0007054-T01-IM5	Lung Adenocarcinoma	*L755A*		Missense	Diploid	35	0.34	2
P-0000163-T02-IM3	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.24	3
P-0000594-T01-IM3	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Amp		0.30	5
P-0002000-T01-IM3	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.09	1
P-0002000-T02-IM5	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.27	4
P-0002876-T01-IM3	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.33	4
P-0004045-T01-IM3	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.30	6
P-0004472-T01-IM5	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.30	15
P-0005562-T01-IM5	Lung Adenocarcinoma	*Y772_A775dup*		IF ins	Diploid		0.28	4

Mutations in lung adenocarcinoma: All mutations

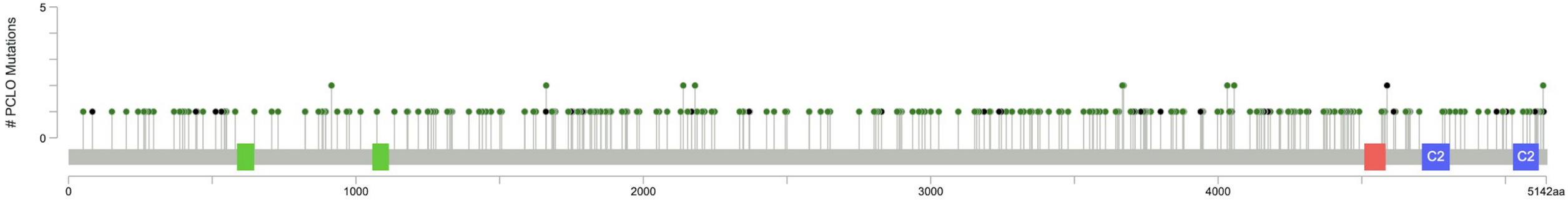


Mutations in lung adenocarcinoma + driver/VUS annotation

Mutations in lung adenocarcinoma: Driver mutations only

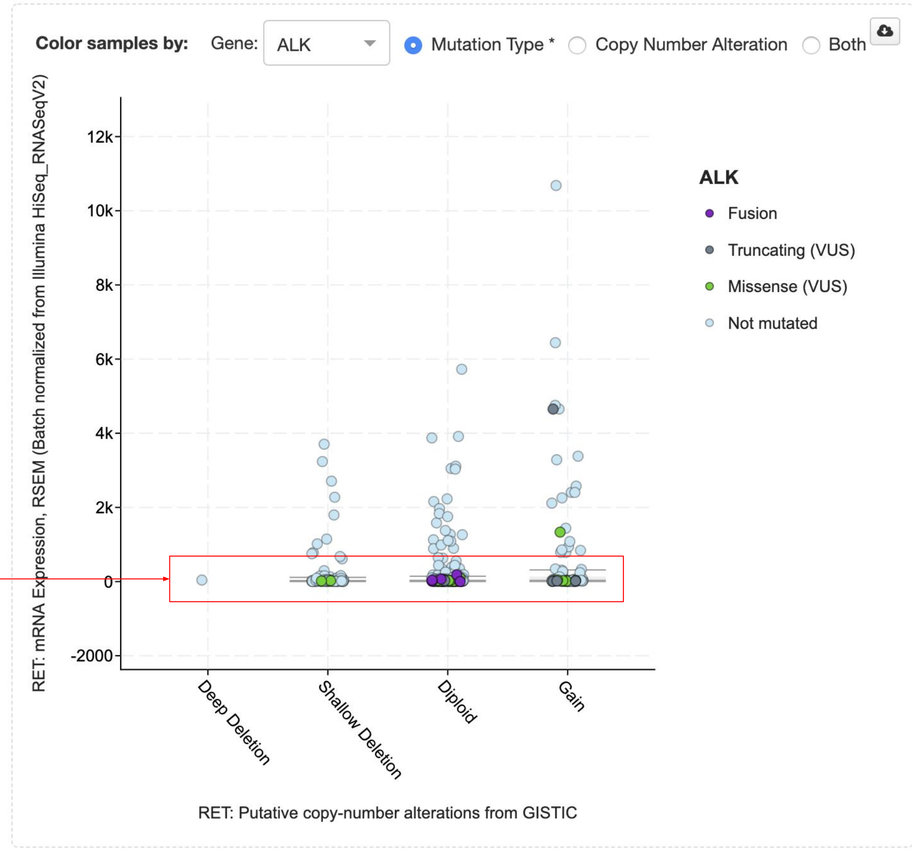


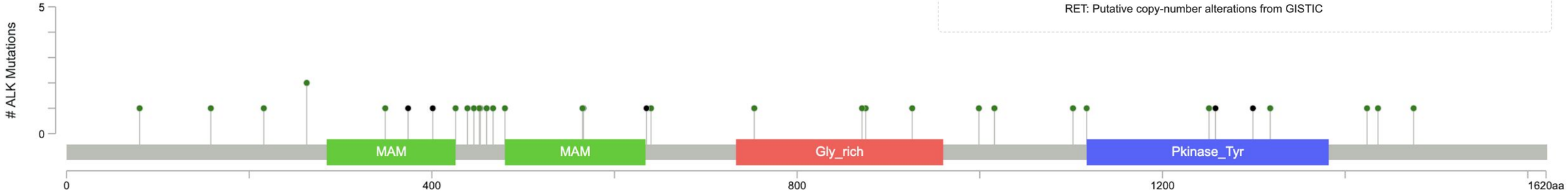
Example: PCLO, a very long gene, mutated in 19%



Example: ALK

- long gene
- often not expressed
- mutations tend to occur in samples with low or no expression



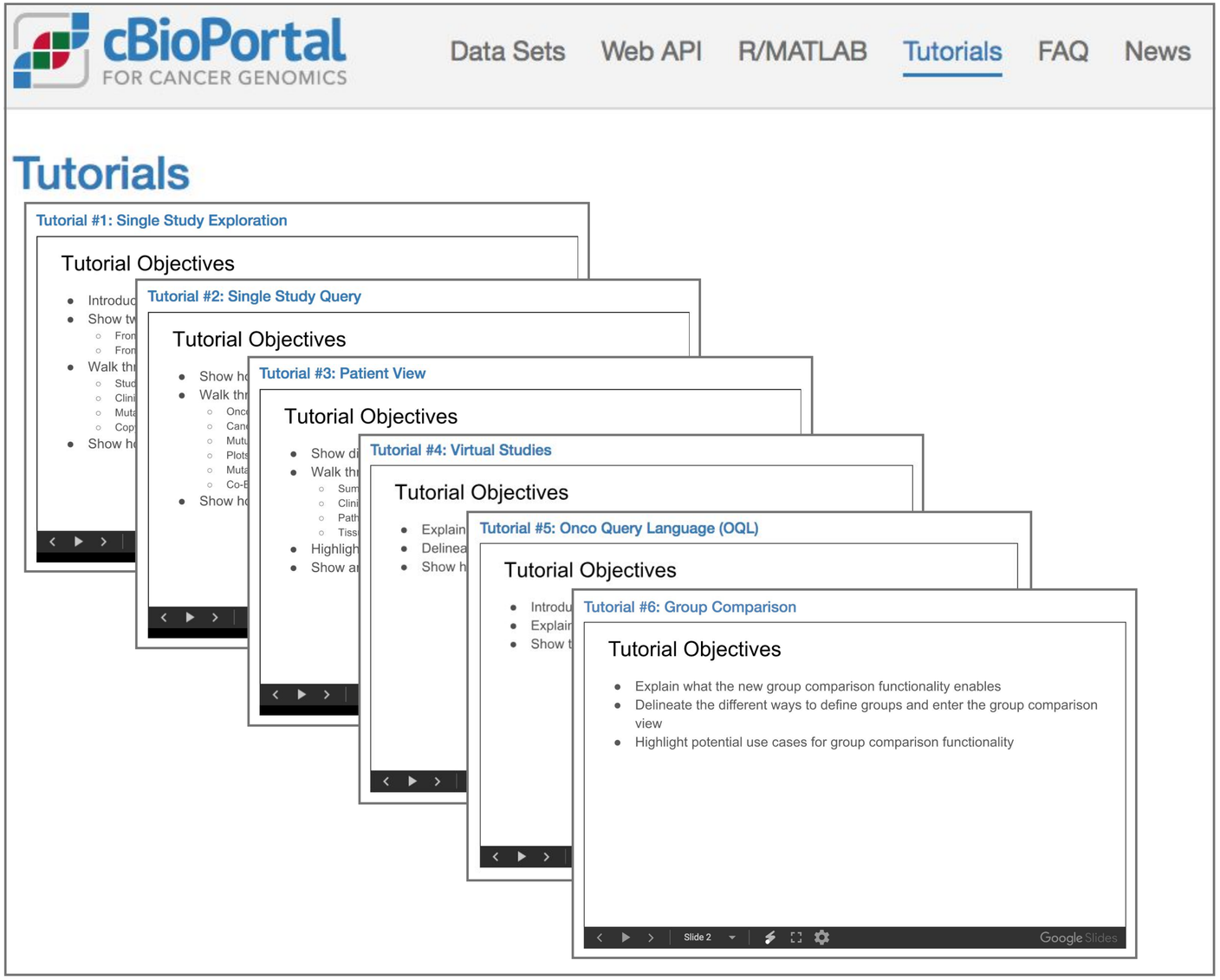


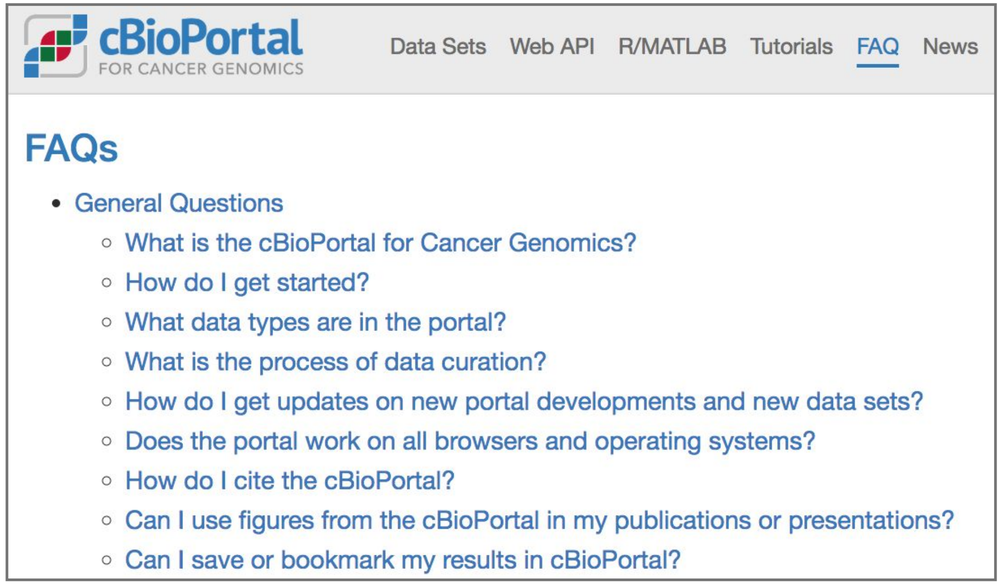
cBioPortal for Cancer Genomics

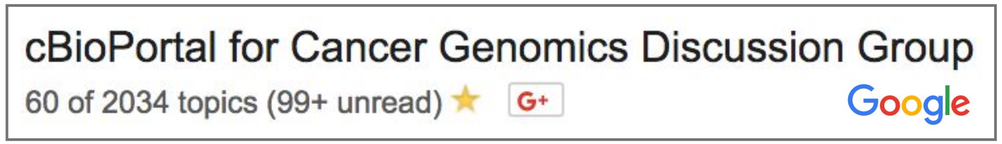
https://www.cbioportal.org/

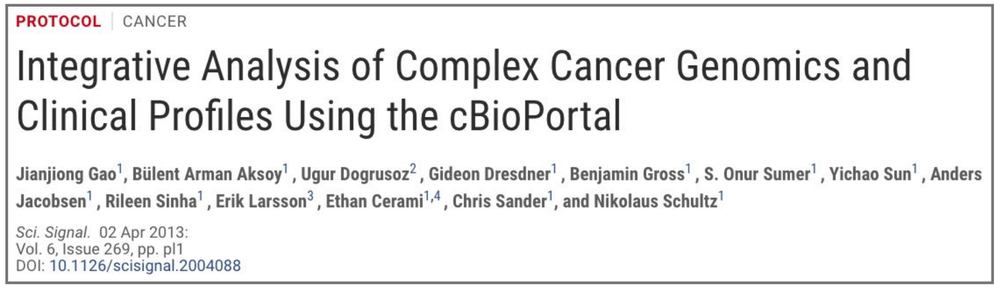
Getting help

cBioPortal for Cancer Genomics



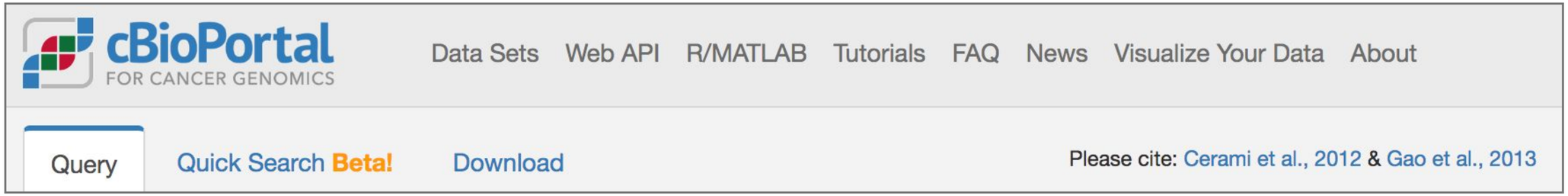






Using cBioPortal for publication

- **Please use cBioPortal in your publications!**
  - Figures are downloadable as PDF/SVG so you can customize them
- Cite the studies that generated the data you are using (if applicable)
- Cite cBioPortal



Questions?

cBioPortal for Cancer Genomics

- Join us for the remaining webinars
- The recording of all webinars will be posted on https://cbioportal.org/tutorials/
- If you still have questions, please ask them via our Google Group

Webinar Schedule

- April 30: Introduction to cBioPortal
- May 7: Mutation Details & Patient View
- **May 14: OQL & Expression**
- **May 21: Group Comparison**
- **May 28: API & R Client**

All webinars are on Thursdays 11am-12pm EDT