Journal club

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Resource

Cell

A Landscape of Pharmacogenomic Interactions in Cancer

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ARTICLE

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Systematic identification of genomic markers of drug sensitivity in cancer cells

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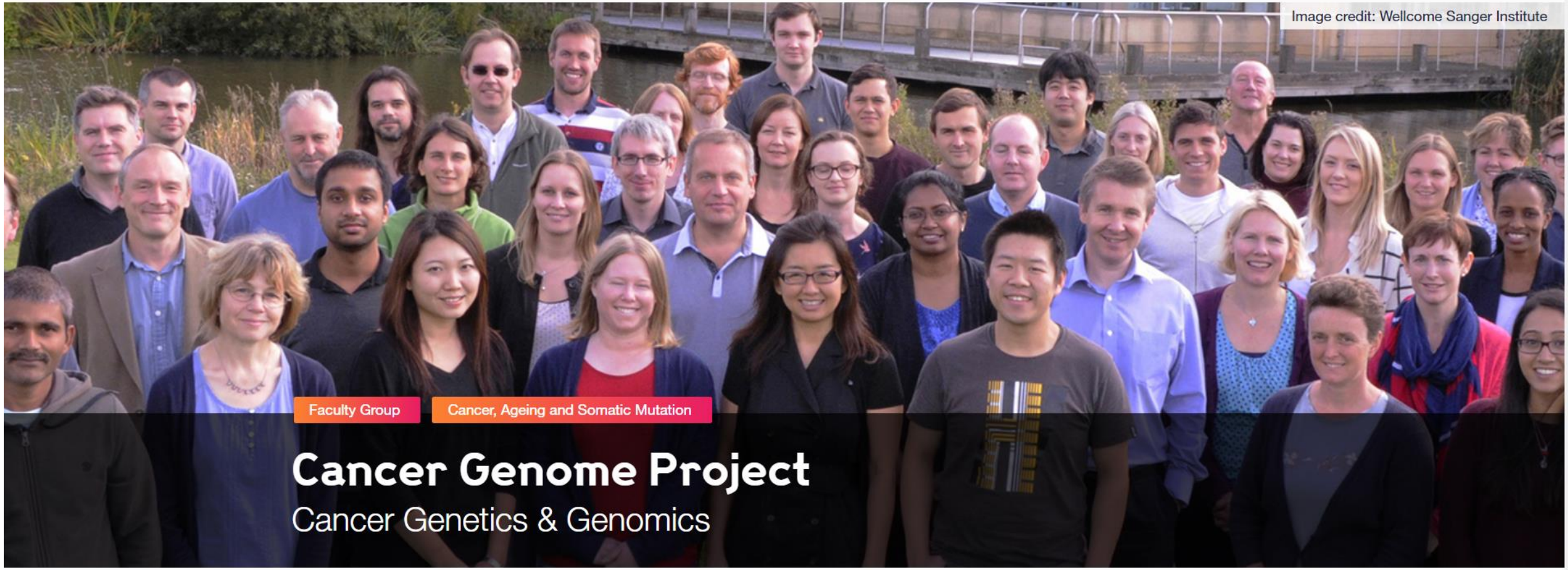
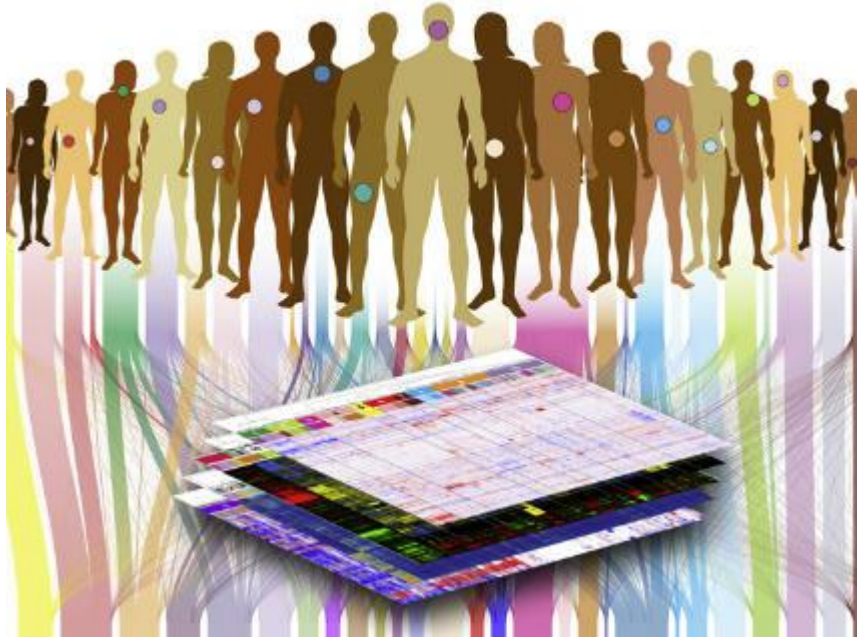


The Cancer Genome Project uses high-throughput genome

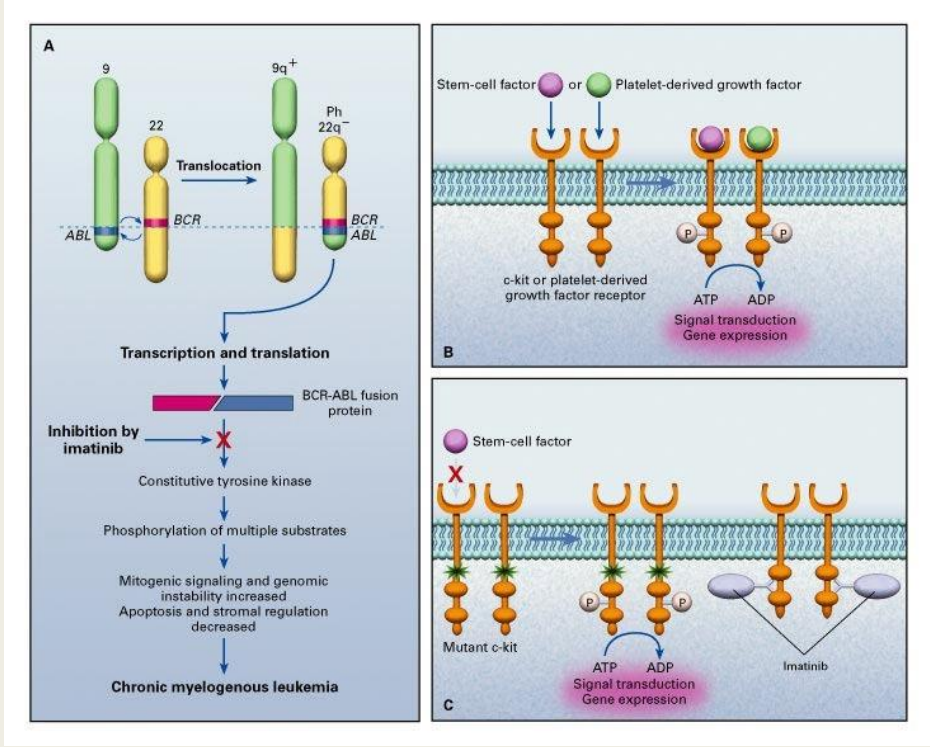
The Cancer Genome Atlas

- Studies from The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC) have generated comprehensive catalogs of the cancer genes involved in tumorigenesis across a broad range of cancer types (Lawrence et al., 2014; Tamborero et al., 2013b; Zack et al., 2013).



Successful examples

- **Imatinib** selectively targets the protein product of the **BCR-ABL translocation** in chronic myeloid leukaemia (CML) has revolutionized the treatment of CML.
- However, a large number of cancer **drugs have not been linked to specific genomic alterations.**
- Systematic methods to identify **predictive biomarkers** during their early development could have a profound effect on the success of new cancer drug development.



EGFR example: low frequency determinants of clinical response

- Clinical responses to small-molecule selective inhibitors of the epidermal growth factor receptor (EGFR), erlotinib and gefitinib were seen in a small fraction of treated patients with non–small-cell lung cancer (NSCLC)
- These are patients with mutations within the EGFR kinase domain (10% to 20% of patients)
- This shows the importance of **stratifying patients** with NSCLC for EGFR TKI therapy based on the mutational status of *EGFR* in their tumors.
- It is also clear that *EGFR* activating mutations **are not the sole determinants of clinical response.**

Table 1. Oncogenic Kinases As Therapeutic Targets in Cancer

Kinase	Alteration	Tumor Types	Therapeutic Agent	Study
Receptor tyrosine kinases				
EGFR	Mutation, amplification	Lung, GBM	Gefitinib, erlotinib	Lynch et al[24]
ErbB2/HER2	Amplification	Breast	Lapatinib	Gomez et al[20]
FGFR1	Translocation	CML	PKC412, BIBF 1120	Hilberg et al[22]
FGFR2	Amplification, mutation	Gastric, breast, endometrial	PKC412, BIBF 1120	Hilberg et al[22]
FGFR3	Translocation, mutation	Multiple myeloma	PKC412, BIBF 1120	Hilberg et al[22]
PDGFRα	Mutation	GBM, GIST	Sunitinib, sorafenib, imatinib	Cohen et al,[17] Demetri et al[18]
PDGFRβ	Translocation	CMML	Sunitinib, sorafenib, imatinib	Cohen et al,[17] Demetri et al[18]
ALK	Mutation/amplification	Lung, neuroblastoma, ALCL	PF-2341066	Christensen et al[16]
MET	Amplification	Gefitinib-resistant NSCLC, gastric	PF-2341066, XL184, SU11274	Salgia et al,[26] Zou et al[30]
IGF-1R	Activation by IGF-II ligand	Colorectal, pancreatic	CP 751 871, AMG479	Hewish et al[21]
c-KIT	Mutation	GIST	Sunitinib, imatinib	Demetri et al[18]
FLT3	Internal tandem duplication	AML	Lestaurtinib, XL999	Illmer and Ehninger[23]
RET	Mutation, translocation	Thyroid medullary carcinoma	XL184	Salgia et al[26]
Nonreceptor tyrosine kinases				
Abl	Translocation (Bcr-Abl)	CML	Imatinib	Druker et al[19]
JAK2	Mutation (V617F), translocation	CML, MPD	Lestaurtinib, INCB018424	Verstovsek et al[28]
Src	Overexpression	NSCLC, ovarian, breast, sarcoma	KX2-391, dasatinib, AZD0530	Blume-Jensen et al[14]
Serine/threonine/lipid kinases				
BRAF	Mutation (V600E)	Melanoma, colon	SB-590885, PLX-4720, RAF265, XL281	Smalley and Flaherty[27]
Aurora kinase A and B	Overexpression	Breast, colon, leukemia	MK-5108 (VX-689)	Warner et al[29]
Polo-like kinases	Overexpression	Breast, lung, lymphoma, colon	BI2536, GSK461364	Warner et al[29]
mTOR	Increased activation	Renal cell carcinoma	Temsirolimus (CCI-779), BEZ235	Chan et al,[15] Maira et al[25]
PI3K	PIK3CA mutations	Colorectal, breast, GBM, gastric	BEZ235	Maira et al[25]

- McDermott et al 2019 JCO

Predictive biomarkers

- Systematic studies of **cancer genomes** have provided unprecedented insights into the **molecular nature of cancer**.

- Clinical responses to anticancer therapies are often restricted to a subset of patients.

- **Predictive biomarkers**: In some cases, **mutated cancer genes** are **potent biomarkers** for **response or resistance to targeted agents**.

- By linking drug activity to the functional complexity of cancer genomes, **systematic pharmacogenomic** profiling in cancer cell lines provides a powerful **biomarker discovery platform to guide rational cancer therapeutic strategies**.

Pharmacogenomics

- Pharmacogenomics: the study of how **genes** affect a person's **response to drugs**.
- This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop **effective**, **safe** medications and **doses** that will be tailored to a person's genetic makeup.
- **Pharmacogenetics**: how variation **in one single gene influences the response to a single drug**.
- **Pharmacogenomics**: a broader term, which studies how all of the genes (the genome) can influence responses to drugs.

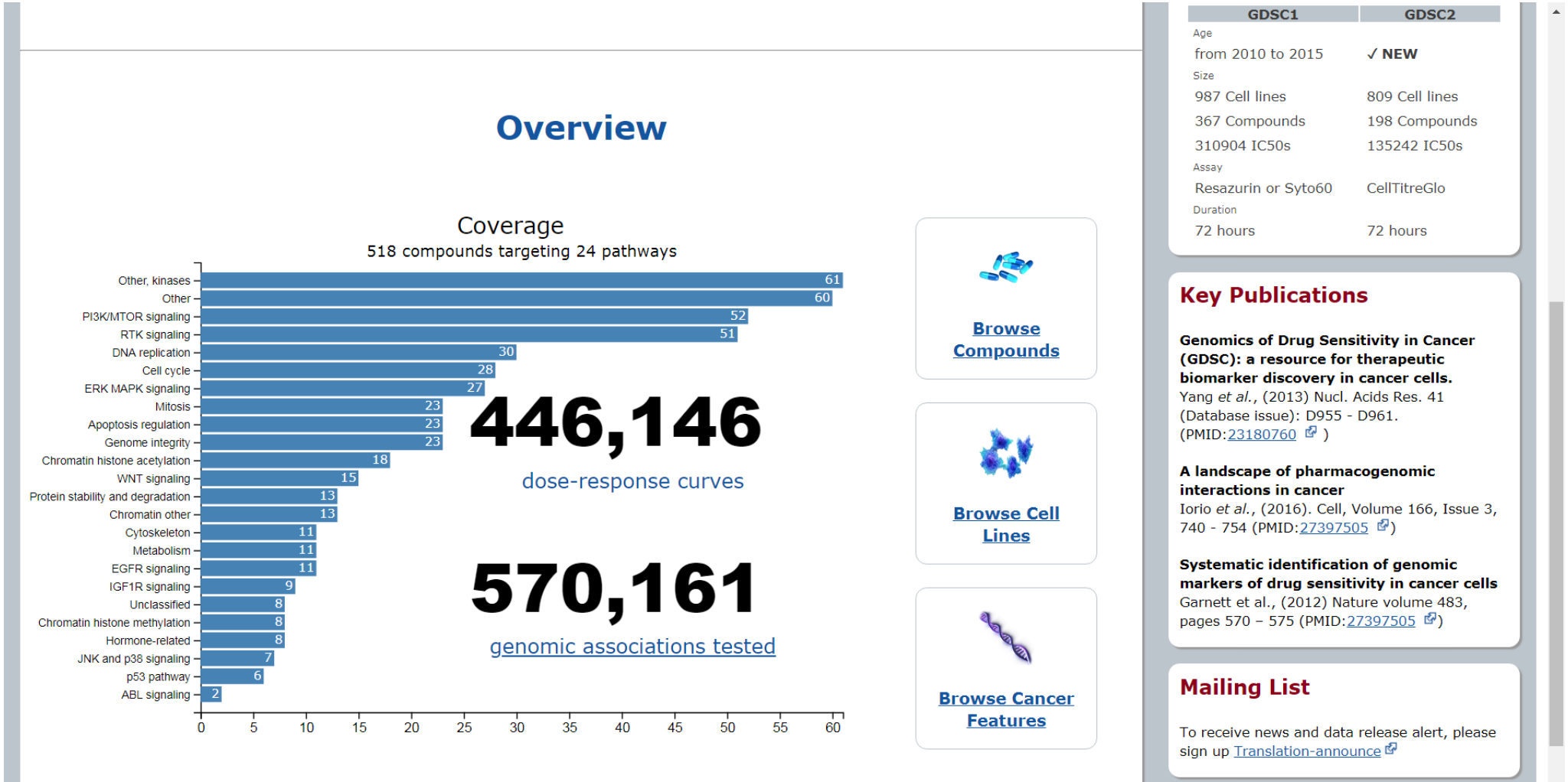
The Genomics of Drug Sensitivity in Cancer

- The Genomics of Drug Sensitivity in Cancer Project is a collaboration between the **Cancer Genome Project** at the **Wellcome Sanger Institute (UK)** and the **Center for Molecular Therapeutics**, **Massachusetts General Hospital Cancer Center** (USA). This work is funded by Wellcome.

Primary tumors: Cancer genomic alterations identified in **11,289 tumors** from 29 tissues (Somatic mutations, Copy number alterations, DNA methylation)

Cancer cells: 1,001 molecularly annotated human cancer cell lines

Drugs: 518 drugs were tested on cells



- Classic **oncogene addiction** paradigms were modified by additional tissue-specific or expression biomarkers.

- We find that cell lines faithfully recapitulate oncogenic alterations identified in tumors, find that many of these **associate with drug sensitivity/resistance**, and highlight the importance of **tissue lineage in mediating drug response**.

- We found that **mutated cancer genes were associated with cellular response** to most currently available cancer drugs.

- Our analysis and datasets are rich resources to link **genotypes with cellular phenotypes** and to identify therapeutic options for selected cancer sub-populations.

Gene-drug interactions in cancer cells in vitro

- Clinical trials are complex and expensive, and **pre-clinical data** that helps stratify patients can dramatically increase the likelihood of success during clinical development (Cook et al., 2014; Nelson et al., 2015).

- Thus, pre-clinical biological models that, as much as reasonably possible, **capture both the molecular features of cancer and the diversity of therapeutic responses** are a necessity.

- Human cancer cell lines are a **facile experimental model** and are widely used for drug development.

- Large-scale **drug sensitivity screens** in cancer cell lines have been used to identify clinically meaningful **gene-drug interactions.**

- In the **past**: imperfect understanding of the landscape of cancer driver genes
- **Now**: view drug sensitivity through the lens of clinically relevant oncogenic alterations

GDSC GOALS

(1) the extent to which **cancer cell lines recapitulate** oncogenic alterations in **primary tumors**

(2) which **oncogenic alterations associate with drug sensitivity**

(3) whether logic **combinations** of multiple alterations better explain drug sensitivity

(4) the relative contribution of **different molecular data types**, either individually or in combination, in **predicting drug response.**

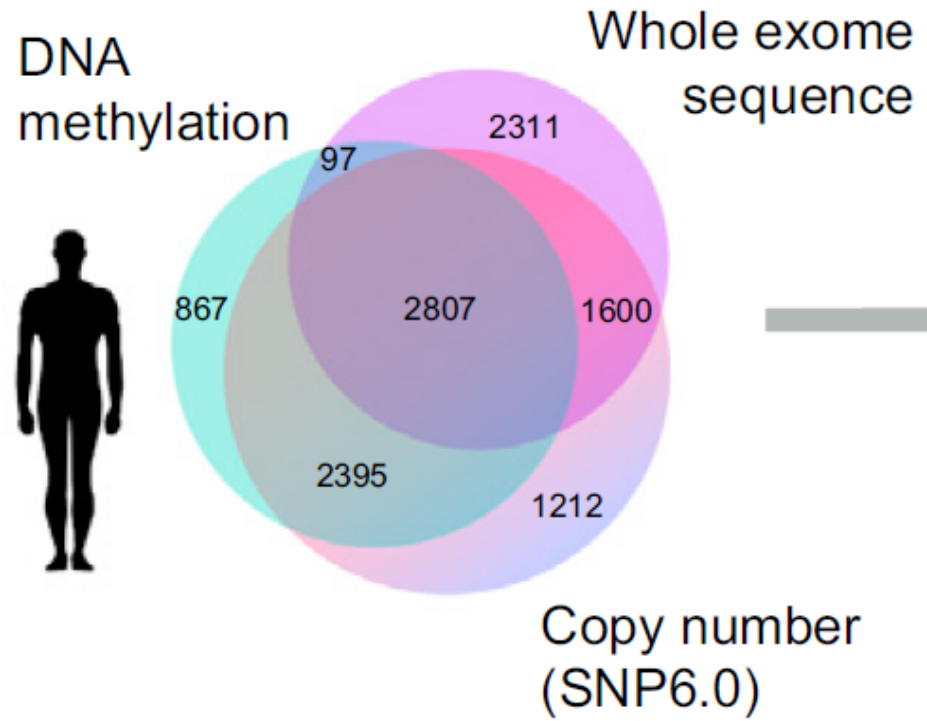
"Cancer functional events" (CFEs)

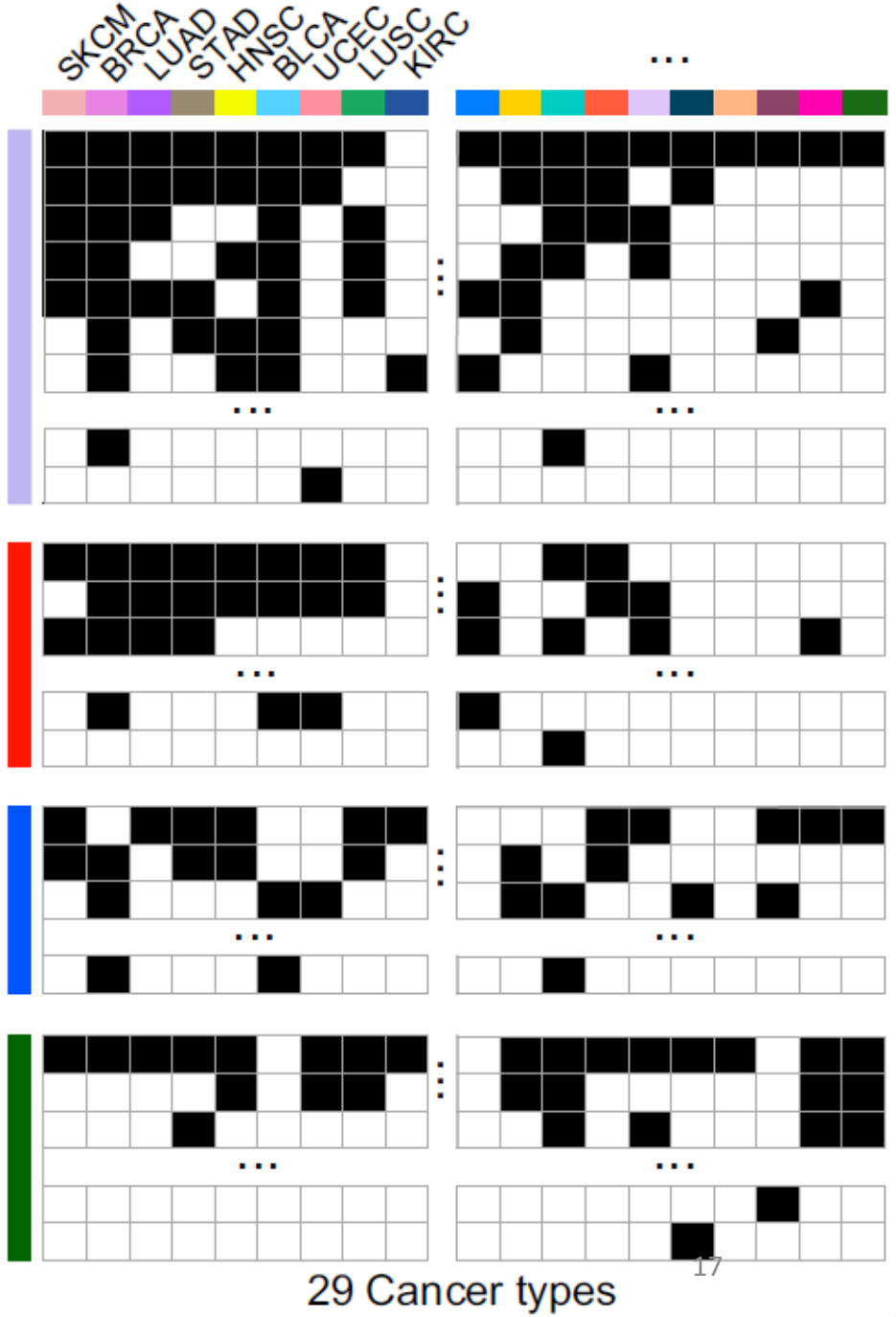
(1) Cancer genes (CGs) for which the mutation pattern in whole-exome sequencing (WES) data is consistent with positive selection

(2) focal recurrently aberrant **copy number** segments (RACSs) from SNP6 array profiles

3) **Hypermethylated** informative 5'C-phosphate-G-3' sites in gene promoters (iCpGs) from DNA methylation data

A Cancer Functional Event (CFE) selection from the analysis of patient tumor data





Multi-omics data from 11,289 Patients

- This identified 461 unique pan-cancer genes.
- We mined the COSMIC database to identify likely driver mutations
- Most tumors harbored only a few driver mutations (median n = 2, range 0–64), consistent with previous reports (Kandoth et al., 2013; Vogelstein et al., 2013).

Recurrently aberrant copy number segments (RACSs)

- 851 cancer-specific RACSs were gained (286 segments) or lost (565 segments), with a median of 19 RACSs per tumor type.
- The median number of genes within each RACS was 15 for amplified regions and one for deleted regions.
- The majority of known driver gene amplifications (e.g., EGFR, ERBB2, MET, and MYC) and homozygous deletions (e.g., CDKN2A, PTEN, and RB1) were captured, with 320 RACSs (38%) containing at least one known putative cancer driver gene, in addition to 531 RACSs (62%) without known driver genes.

- iCpGs were identified using DNA methylation array data for 6,166 tumor samples spanning 21 cancer types.

- We defined 378 iCpGs based on a multimodal distribution of their methylation signal in at least one cancer type (Tables S2H and S2I).
- This also established a discretization threshold used to define such regions as hyper-methylated in the cell lines

- In total, our multidimensional analysis of >11,000 patient tumor samples identified 1,699 cancer-specific CFEs, which were further merged into **1,273 unique pan-cancer CFEs.**

Oncogenic Alterations in Patient Tumors Are Conserved across Cell Lines

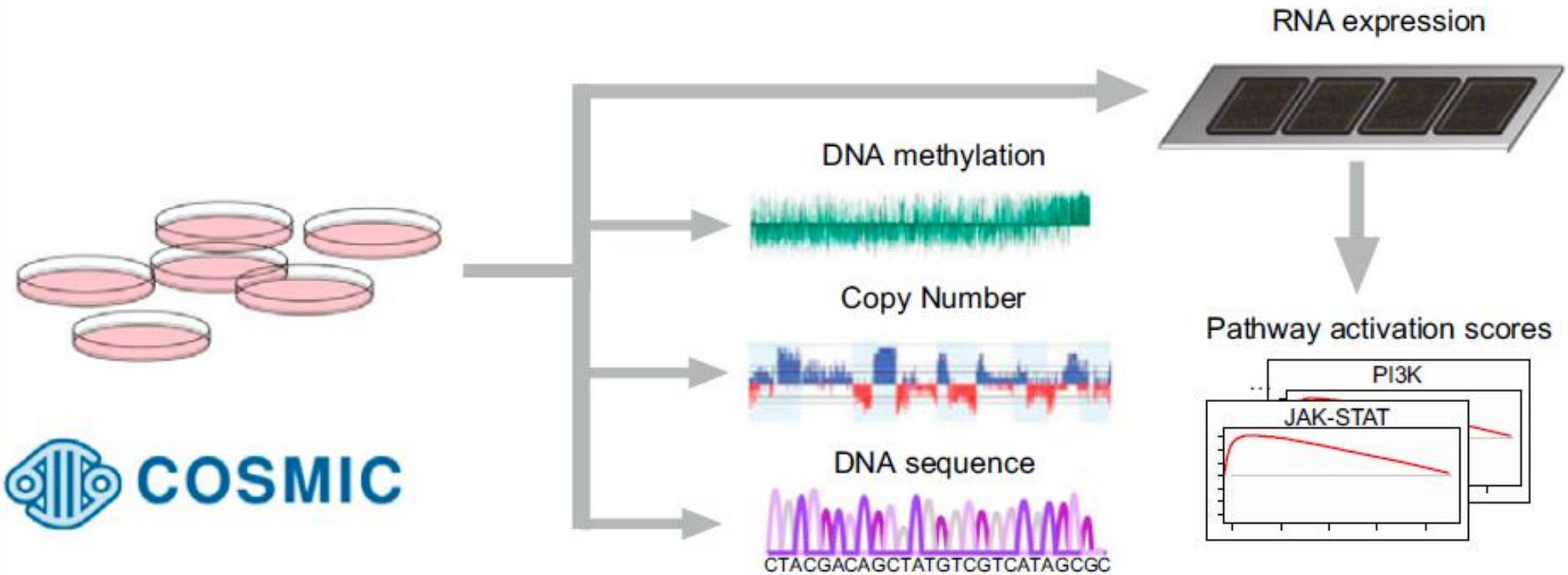
- Next, we assessed the extent to which the mutational landscape of cancer cell lines captures that seen in primary tumors.

- We utilized a panel of 1,001 human **cancer** cell lines analyzed through WES (n = 1,001), copy number (n = 996), gene expression (n = 968), and DNA methylation (n = 957) (https://cancer.sanger.ac.uk/cell_lines/cbrowse/all) and which we reclassified according to the TCGA tissue labels.

- Molecular alterations identified in cell lines were **filtered using the CFEs identified in the primary tumor samples**, providing a set of clinically relevant CFEs for the cell lines (Figure 1C).

Characterization of cancer cell lines

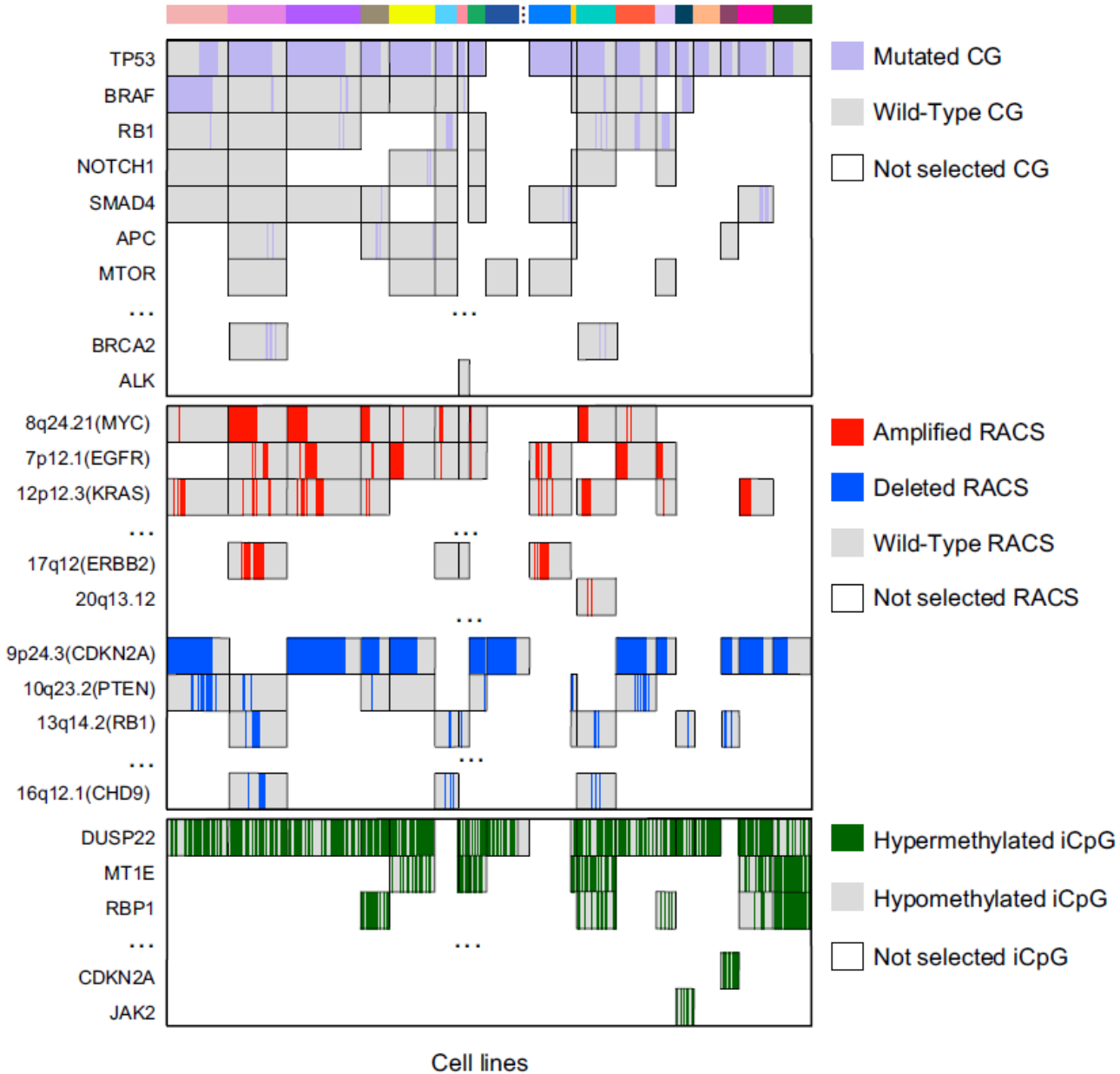
B



Multi-omics data from 1,001 Cell lines

C

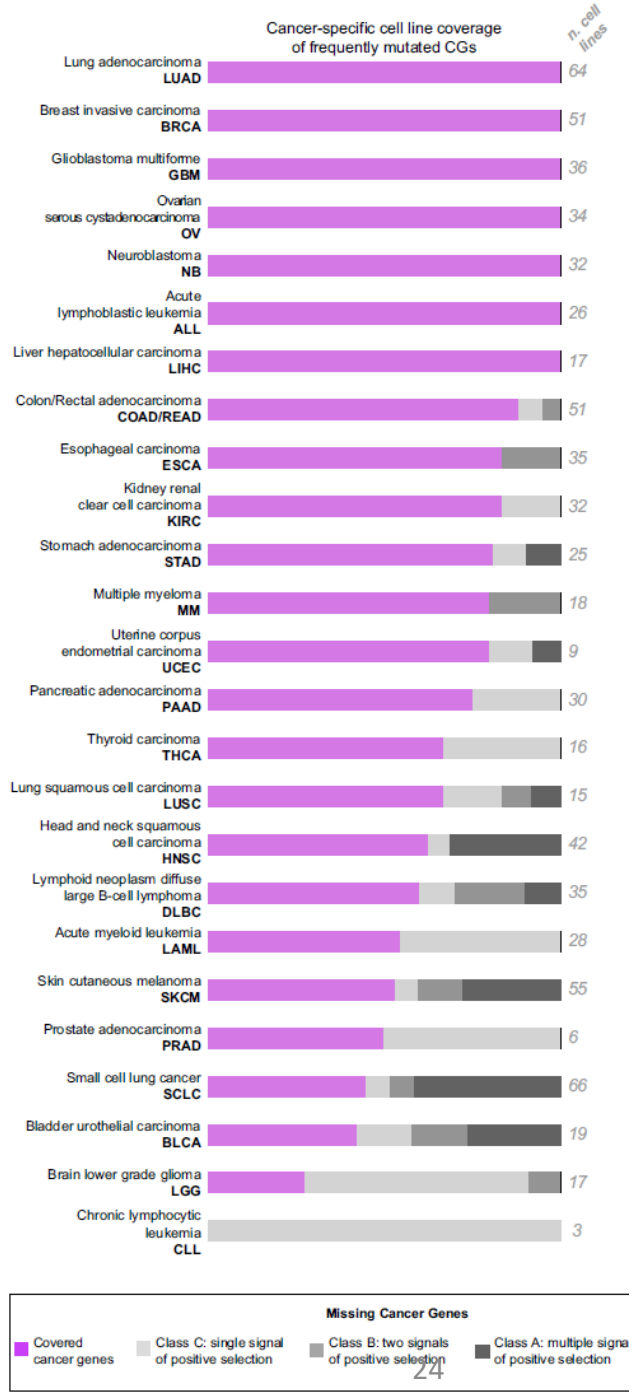
Clinically relevant CFEs in cancer cell lines



Multi-omics CFE status matrix in cell lines

CFEs in cell lines

- Of the 1,273 pan-cancer CFEs identified in patient tumors, **1,063 (84%) occurred in at least one cell line**, and 1,002 (79%) occurred in at least three (Figure 2A).
- This concordance was greatest for the RACSs (100% of 425), followed by iCpGs (338 of 378, 89%) and CGs (300 of 470).
- When considering cancer-specific CFEs, concordance was highest for CFEs occurring in at least 5% of patients (median of 86% of CFEs covered across cancer types).
- Coverage of CFEs varied by cancer type.



- Alterations in **13 canonical cancer-associated pathways** was **highly correlated** between cell lines and tumors of the same cancer type.

(See Excel file)

A

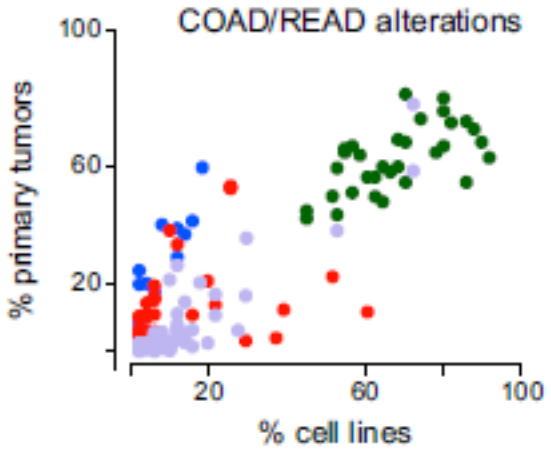
	LAML		COAD/READ		OV		KIRC		LUAD		GBM		HNSC		THCA		LGG		BRCA		BLCA		SKCM		UCEC		STAD		PRAD		LUSC	
Cell cycle		4	52	29	42	39	17	93	53	81	91	91	72	80	1	7	25	81	32	43	45	67	51	82	33	44	47	58	9	40	57	87
DNA repair	3		34	18	8	18	2		10	2	5		4	2	1		37		39	59	8		7	2	9	22	5	8	4	20	6	
Histone modifier	5	29	32	37	10	39	39	46	22	20	2	9	35	29	2		10	13	8	18	68	56	11	15	46	56	17	21	4	40	23	33
Other growth/proliferation signaling																	4	13	17	22											23	20
PI3K-AKT-MTOR signaling		4	58	41	5	33	9	7	16	22	33	59	19	22	1	21	13	25	46	59	22	11	13	16	82	89	32	25	32	60	32	33
RAS-RAF-MEK-ERK/JNK signaling	17	54	85	84	27	73	1	4	50	48	17	35	13	12	70	93	10	25	32	45	9	22	87	100	23	44	40	33	1	20	15	33
RTK signaling family	3		43	10	4	6	1		25	25	84	35	18	27			21	38	33	59	29	11	2		22	33	15	17	1		38	20
Survival/cell death regulation signaling			14	2	0				1				4	15	1				6	8	2		1		1		12	8	26	40	12	13
Telomere maintenance					10	3			29	19									6	20			8	2	9						35	33
TGF-beta signalling			69	45	0	15	1		4				2	15			1		1		1				1		16	13	1		2	
TP53 signaling	8	67	67	78	93	79	18	100	63	92	92	100	77	98	1	79	62	100	48	84	49	83	50	98	27	78	52	88	25	100	86	100
Transcription factor regulation	17	13	36	47	25	33	42	43	12	19	1		6	2	1	14	1	6	28	37	28	39	4	13	38	78	21	29	2	20	69	33
WNT signaling		4	90	88	2	15		7	6	6	1		4	5	1				1	4	15		6	5	39	44	14	29	4	20	6	7

Tumors
Cell lines
n = % altered samples
100
50
0

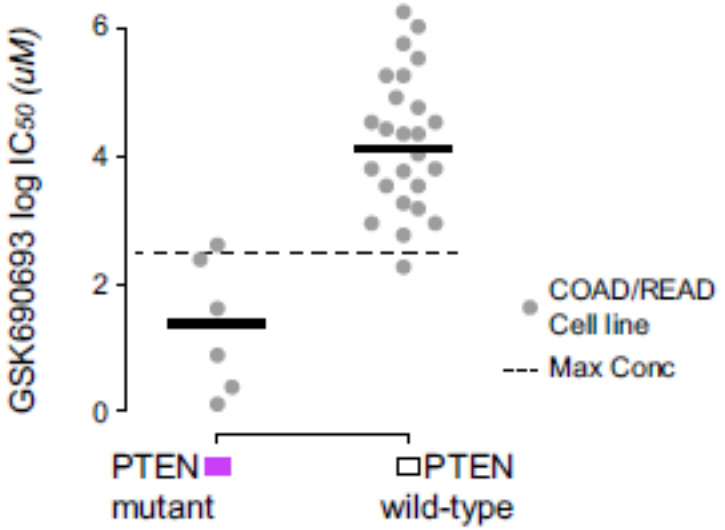
4D

Analyses

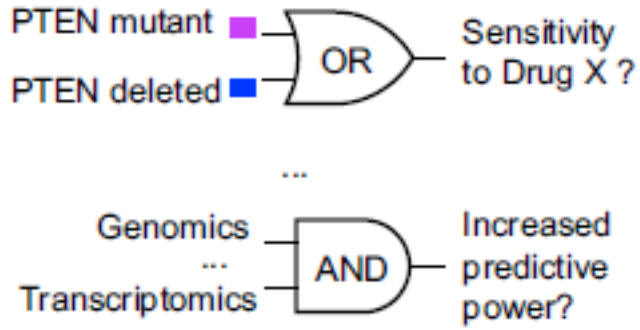
1. Comparison of cell lines and primary tumors across cancer types



2. Identification of clinically relevant markers of drug response



3. Predictive ability assessment of individual CFE/data-type and their combinations



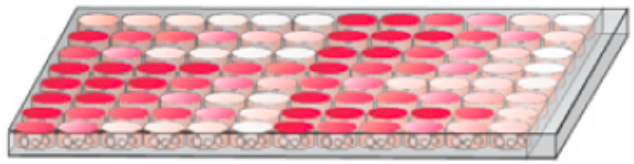
http://www.cancerrxgene.org

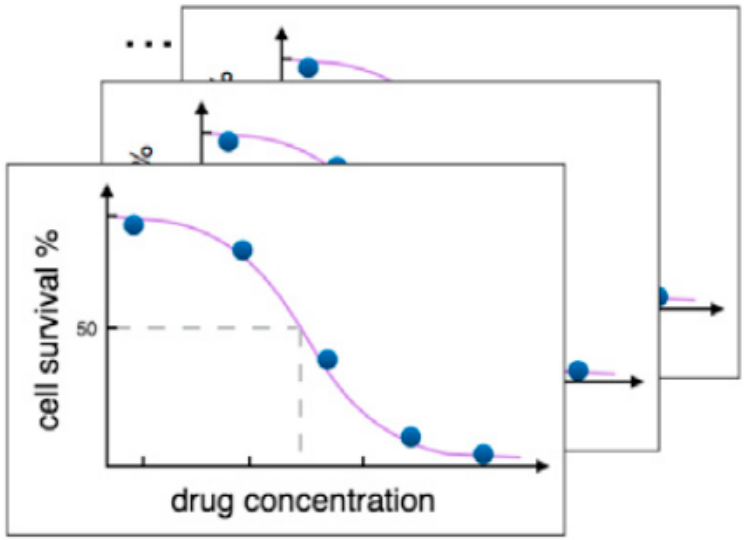
- These results show that a sufficiently large panel of cell lines is able to capture individual clinically relevant genomic alterations, in addition to pathway alterations and global signatures of driver events.

A Therapeutic Landscape of Human Cancers Modeling Pharmacogenomic Interactions

- To investigate how CFEs detected in primary tumors impact drug response.
- Cell lines underwent extensive drug sensitivity profiling.
- The effect of each drug on cell number was used to model sensitivity as IC50 (drug concentration that reduces viability by 50%) or AUC (area under the dose-response curve) values (Tables S4A and S4B).

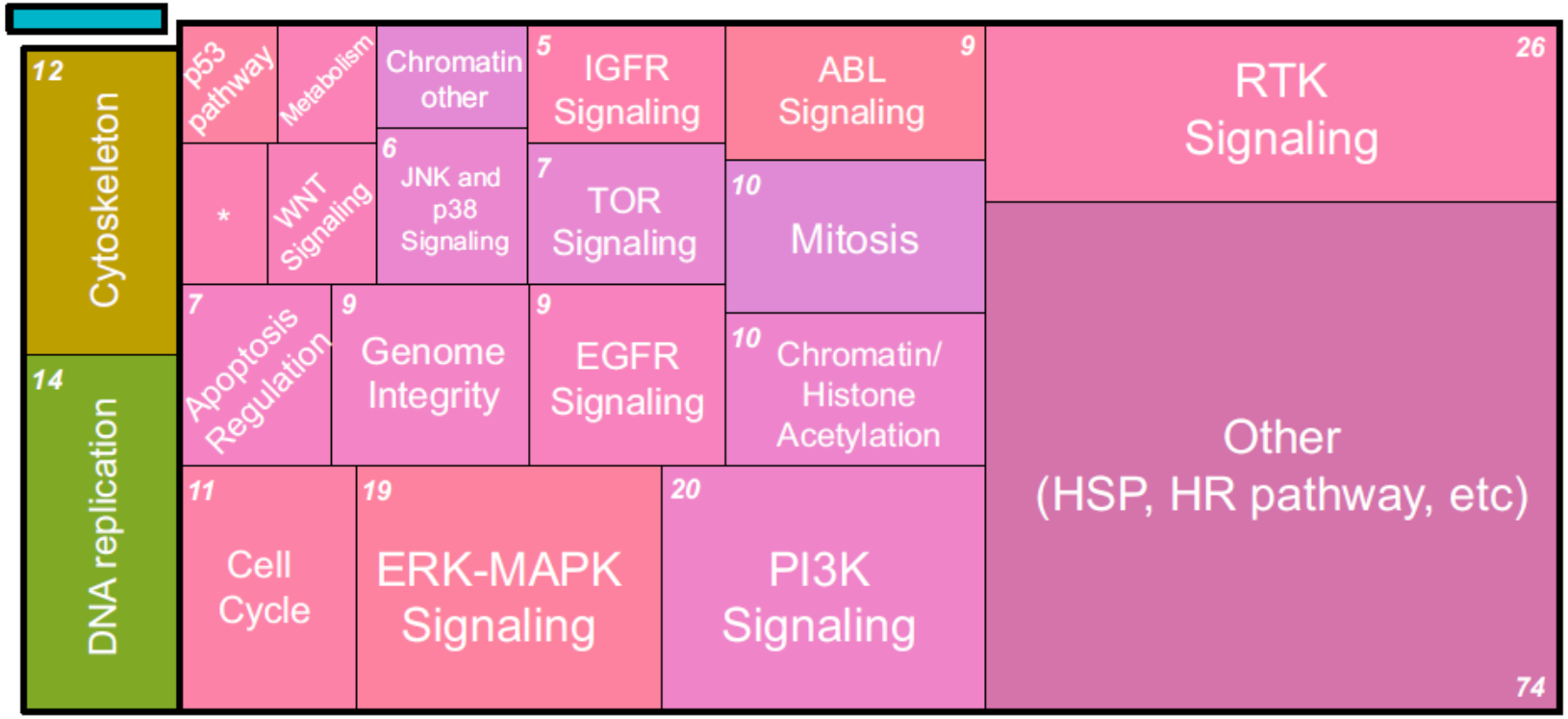
Drug screening





1 compound

265 Compounds



cytotoxic

targeted

212,774 Compound/Cell line dose-response curves

* Chromatin/Histone Methylation

- Screened compounds included **cytotoxics (n = 19)** and **targeted agents (n = 242)** selected against **20 key pathways** and cellular processes in cancer biology

- These 265 compounds include clinical drugs (n = 48), drugs currently in clinical development (n = 76), and experimental compounds (n = 141).

Cell viability assays

- Cells were seeded in either 96-well or 384-well microplates in medium supplemented with 5% FBS and penicillin/streptavidin.
- The optimal cell number for each cell line was determined to ensure that each was in growth phase at the end of the assay (**70% confluency).**
- Adherent cell lines were plated 1 day before treatment with a **9-point twofold dilution** series of each compound using liquid handling **robotics**, and assayed at a **72-h time point**.
- Cells were fixed in **4% formaldehyde** for 30 min and then stained with 1 mM of the fluorescent nucleic acid stain **Syto60** (Invitrogen) for 1 h.
- Suspension cell lines were treated with compound immediately following plating, incubated for 72 h, and then stained with 55 mgml **resazurin** (Sigma) prepared in glutathione-free media for 4 h.
- Quantification of fluorescent signal intensity was performed using a fluorescent plate reader at excitation and emission wavelengths of 630/695nM for Syto60, and 535/595nM for resazurin.
- All screening plates were subjected to stringent quality control measures and a Z-factor score comparing negative and positive control wells was calculated.

Datasets

GDSC1	GDSC2
Age	
from 2010 to 2015	✓ **NEW**
Size	
987 Cell lines	809 Cell lines
367 Compounds	198 Compounds
310904 IC50s	135242 IC50s
Assay	
Resazurin or Syto60	CellTitreGlo
Duration	
72 hours	72 hours

- Cluster analysis based on AUC values confirmed that compounds with overlapping nominal targets or targeting the same process/pathway had similar activity profiles (See Excel file, compound clustering)

- We used three distinct analytical frameworks to define the contribution of CFEs to the prediction of drug sensitivity

- ANOVA was used to identify single CFEs as markers of drug response.

- Logic models identified combinations of CFEs that improve the prediction of drug response.

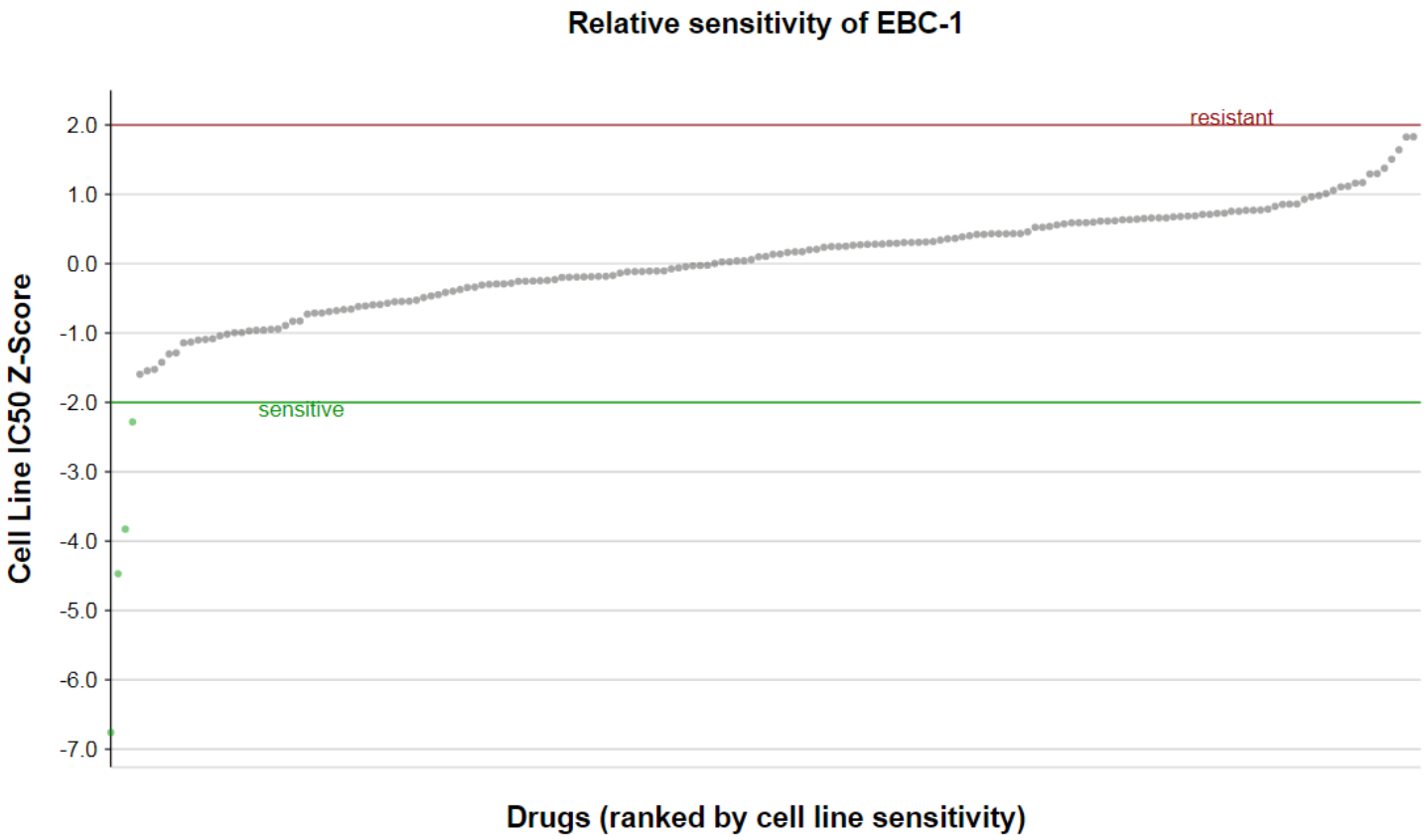
- We used machine-learning algorithms to assess the contribution of each molecular data type (CGs, RACS, iCpGs, and gene expression) in explaining variation in drug response

Cell Line: EBC-1

Link to Cell Model Passport

Dataset

- (•) GDSC2
- ( ) GDSC1



Show 25 entries Filter: Export: CSV TSV

Drug	Targets	Z score
Savolitinib	MET	-6.76119
Foretinib	MET, KDR, TIE2, VEGFR3/FLT4, RON, PDGFR, FGFR1, EGFR	-4.47182
Crizotinib	MET, ALK, ROS1	-3.82787
WEHI-539	BCL-XL	-2.28165
PD0325901	MEK1, MEK2	-1.59562
Trametinib	MEK1, MEK2	-1.54442
Ulixertinib	ERK1, ERK2	-1.52555
Selumetinib	MEK1, MEK2	-1.4214

Genomics of Drug Sensitivity in Cancer

wellcome sanger institute

MASSACHUSETTS GENERAL HOSPITAL CANCER CENTER

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Cancer Feature: EGFR_mut

Dataset ⓘ

- (•) GDSC2
- ( ) GDSC1

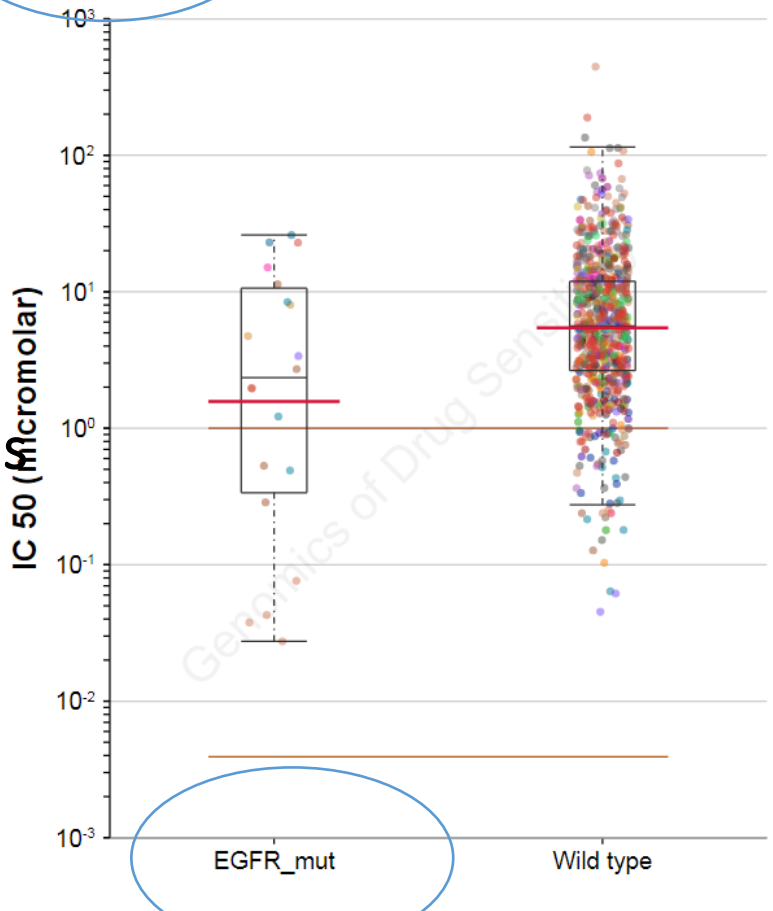
Tissue specific analysis

Pan-Cancer

Volcano Plot | Scatter plots

Osimertinib

Click on circles to link to cell line information



Select Drug

Screening concentration: 0.0039063 (lower brown line) - 1.0000 (upper brown line)

	EGFR_mut	Wild type	MWW p value	Signif	Selected
Number of cell lines	20	701			
Median	2.3424	5.6029			
Geometric mean (red line)	1.5687	5.4293			
Selected groups			0.0252	*	
ALL	2	22	0.10546	-	☑
ACC	0	1	-	-	☑
BLCA	0	18	-	-	☑
BRCA	0	44	-	-	☑
CESC	0	11	-	-	☑
CLL	0	1	-	-	☑
COREAD	4	38	0.13934	-	☑
DLBC	0	18	-	-	☑
ESCA	3	26	0.91446	-	☑
GBM	2	21	0.071814	-	☑
HNSC	0	26	-	-	☑

Drug-gene interactions

Cancer Feature: cnaPANCAN129 show genes

Known Driver Genes: MET

Copy number alternation: gain

Dataset

- (•) GDSC2
- ( ) GDSC1

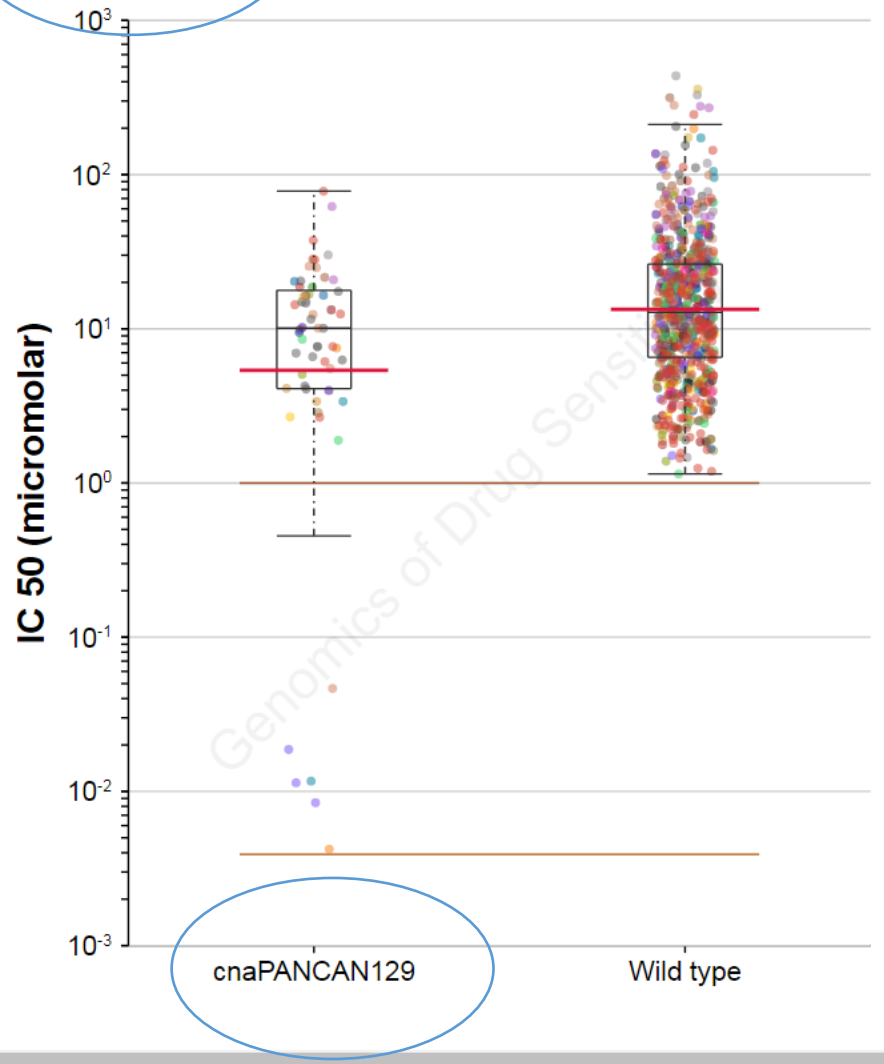
Tissue specific analysis

Pan-Cancer

Volcano Plot | Scatter plots

Savolitinib

Click on circles to link to cell line information



Select Drug

Screening concentration: 0.0039063 (lower brown line) - 1.0000 (upper brown line)

	cnaPANCAN129	Wild type	MWW p value	Signif	Selected
Number of cell lines	58	688			
Median	10.089	12.793			
Geometric mean (red line)	5.3766	13.341			
Selected groups			0.0107	*	
ALL	2	21	0.62344	-	☑
ACC	0	1	-	-	☑
BLCA	0	18	-	-	☑
BRCA	7	37	0.10174	-	☑
CESC	1	12	0.76923	-	☑
CLL	0	2	-	-	☑
COREAD	3	39	0.84512	-	☑
DLBC	1	18	0.73684	-	☑
ESCA	2	27	0.022562	*	☑
GBM	2	22	0.27278	-	☑
HNSC	1	25	0.35064	-	☑
KIRC	2	14	0.066667	-	☑
LIHC	1	12	0.92308	-	☑

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Genomics of Drug Sensitivity in Cancer

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Cancer Feature: EGFR_mut

Dataset

- (•) GDSC2
- ( ) GDSC1

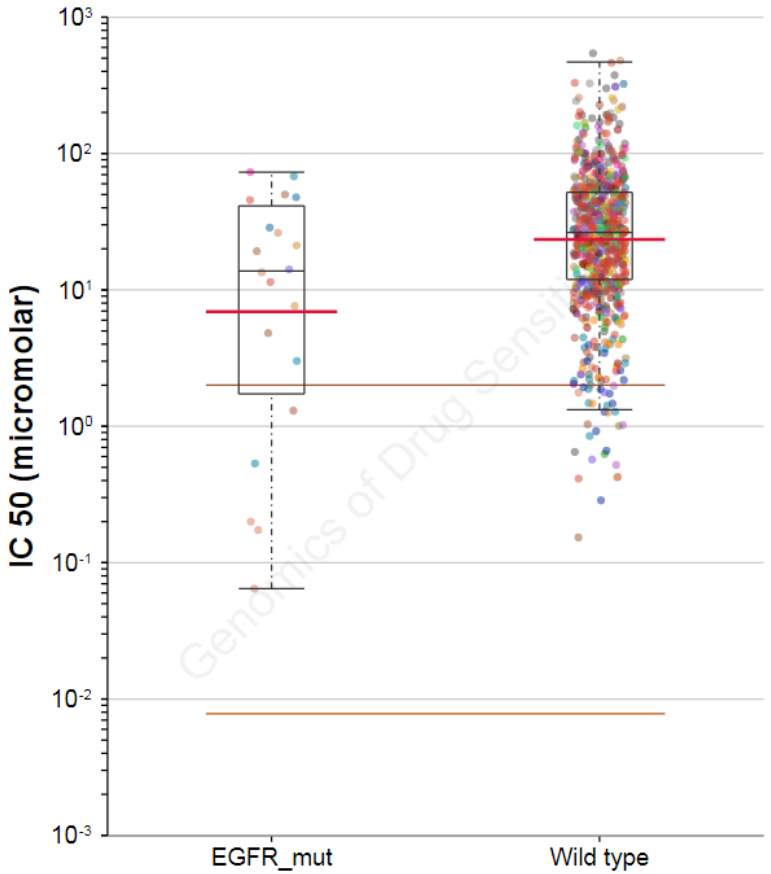
Tissue specific analysis

Pan-Cancer

Volcano Plot | Scatter plots

Gefitinib

Click on circles to link to cell line information



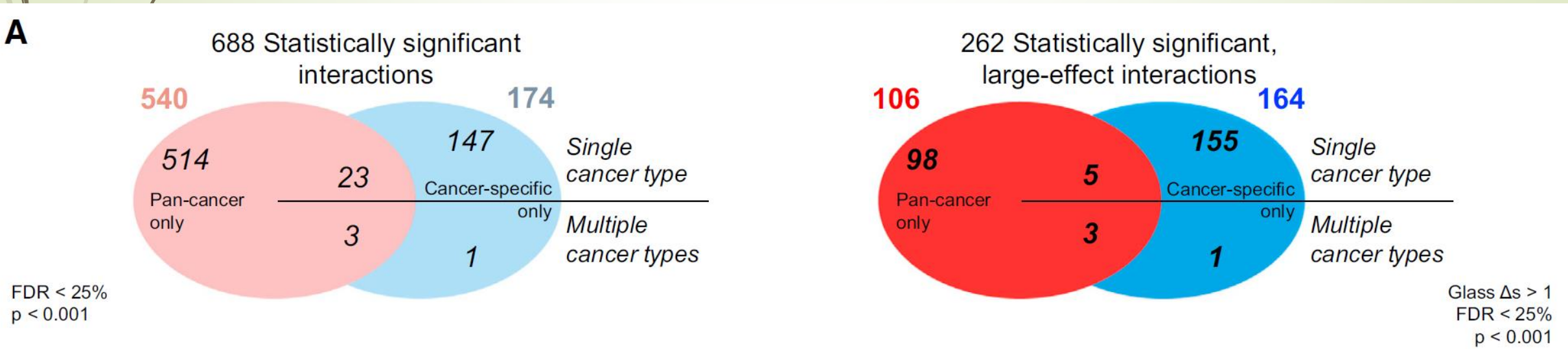
Select Drug

Screening concentration: 0.0078125 (lower brown line) - 2.0000 (upper brown line)

	EGFR_mut	Wild type	MWW p value	Signif	Selected
Number of cell lines	20	701			
Median	13.783	26.343			
Geometric mean (red line)	6.9073	23.390			
Selected groups			0.0160	*	
ALL	2	22	0.95836	-	☑
ACC	0	1	-	-	☑
BLCA	0	18	-	-	☑
BRCA	0	44	-	-	☑
CESC	0	11	-	-	☑
CLL	0	1	-	-	☑
COREAD	4	38	0.17710	-	☑
DLBC	0	18	-	-	☑
ESCA	3	26	0.74726	-	☑
GBM	2	21	0.70254	-	☑
HNSC	0	26	-	-	☑
KIRC	0	14	-	-	☑
LIHC	0	15	-	-	☑

ANOVA Analysis Defines a Landscape of Pharmacogenomic Interactions

- For pan-cancer ANOVA, the set of CFEs included 267 CGs, 407 RACSs, and three gene fusions (BCR-ABL, EWSR1-FLI1, and EWSR1-X).
- Overall, for the 265 compounds, we identified 688 statistically significant interactions between unique CFE-drug pairs (p value < 103 at a false discovery rate [FDR] < 25%; Figure 4A), with 540 pan-cancer and 174 cancer-specific hits.
- A subset of 262 CFE-drug pairs was additionally defined as large-effect interactions.



Cancer Feature: cnaPANCAN129 show genes

Known Driver Genes: MET

Copy number alternation: gain

Dataset

- (•) GDSC2
- ( ) GDSC1

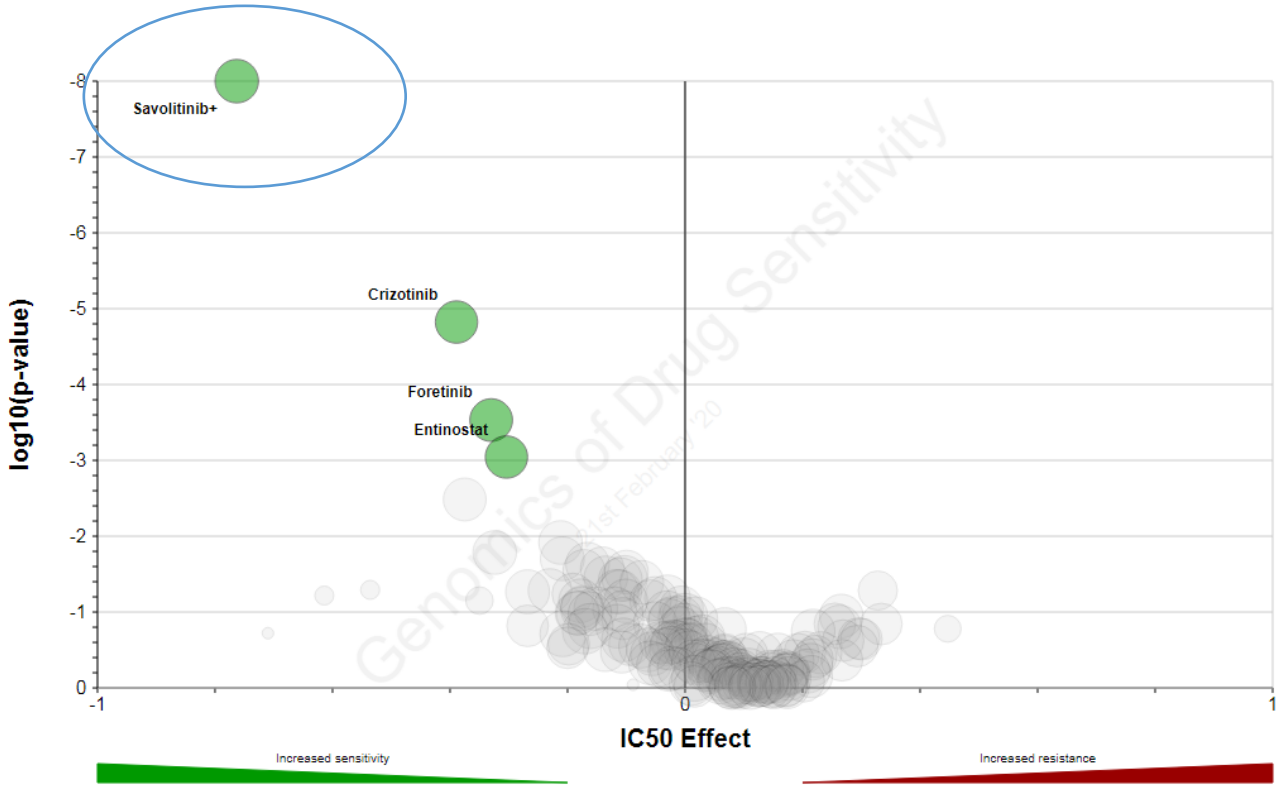
Tissue specific analysis

Pan-Cancer

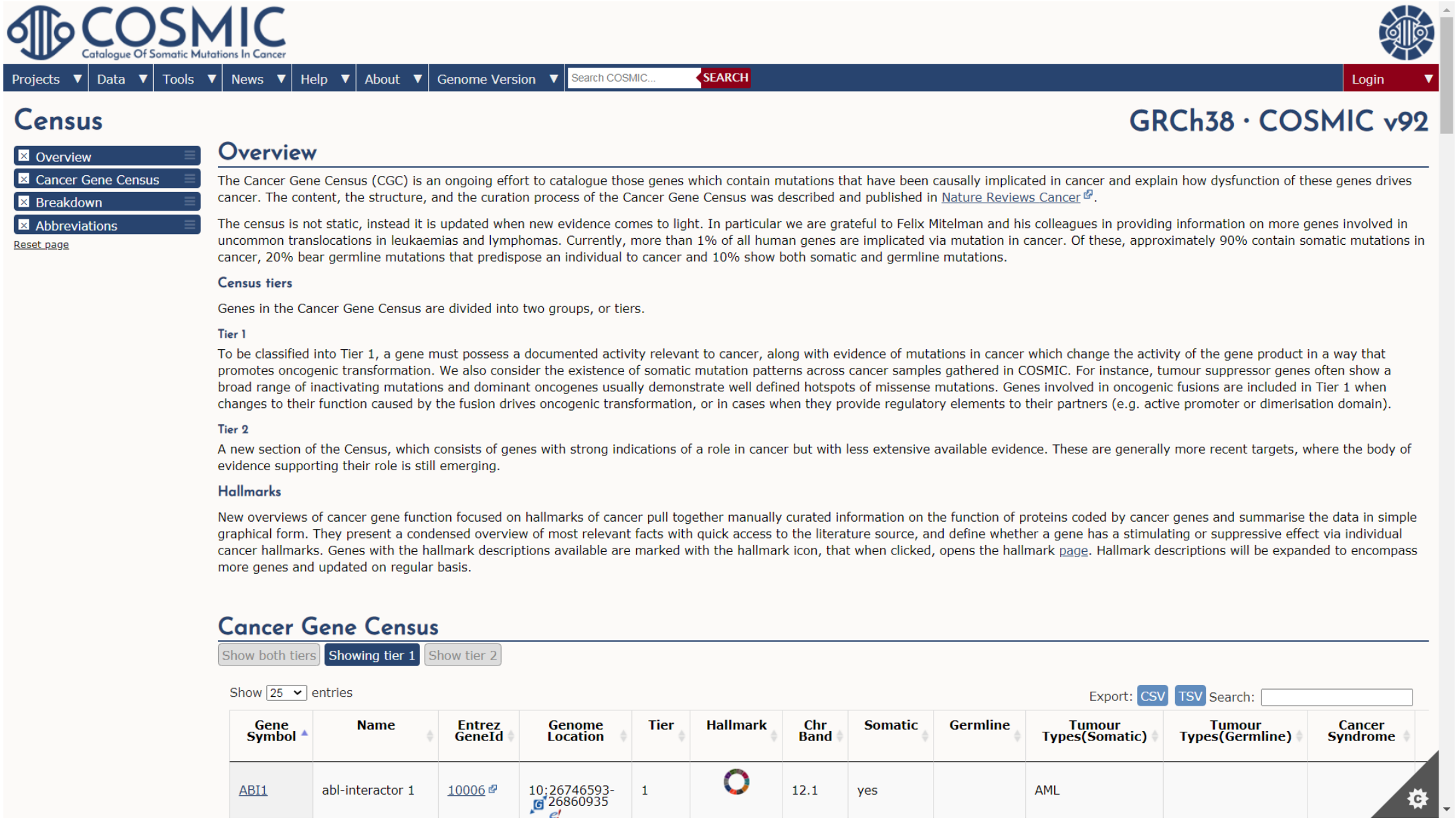
Volcano Plot | Scatter plots

Tissue analysis | Combined analysis

Each circle represents an association between a genomic marker and drug sensitivity analysed using ANOVA. Different ANOVA analyses use selected context specific genomic markers as features. Use the dropdown to select a tissue specific analysis or a pan-cancer analysis.



Drug	Drug Target	Effect size	P-value	FDR%	No. of altered cell lines	Tissue analysis
Savolitinib	MET	-0.763	1.27e-11	8.47e-07	58	PANCANCER
Crizotinib	MET, ALK, ROS1	-0.389	1.5e-05	0.809	55	PANCANCER
Foretinib	MET, KDR, TIE2, VEGFR3/FLT4, RON, PDGFR, FGFR1, EGFR	-0.33	0.000294	9.75	56	PANCANCER
Entinostat	HDAC1, HDAC3	-0.304	0.000904	8.29	55	PANCANCER
GNF-317	PI3Kalpha	-0.375	0.00328	27.5	56	PANCANCER


COSMIC
Catalogue Of Somatic Mutations In Cancer
Projects
Data
Tools
News
Help
About
Genome Version
Search COSMIC...
SEARCH
Login
Census
GRCh38 · COSMIC v92
Overview
Cancer Gene Census
Breakdown
Abbreviations
Reset page
Overview
The Cancer Gene Census (CGC) is an ongoing effort to catalogue those genes which contain mutations that have been causally implicated in cancer and explain how dysfunction of these genes drives cancer. The content, the structure, and the curation process of the Cancer Gene Census was described and published in Nature Reviews Cancer.
The census is not static, instead it is updated when new evidence comes to light. In particular we are grateful to Felix Mitelman and his colleagues in providing information on more genes involved in uncommon translocations in leukaemias and lymphomas. Currently, more than 1% of all human genes are implicated via mutation in cancer. Of these, approximately 90% contain somatic mutations in cancer, 20% bear germline mutations that predispose an individual to cancer and 10% show both somatic and germline mutations.
Census tiers
Genes in the Cancer Gene Census are divided into two groups, or tiers.
Tier 1
To be classified into Tier 1, a gene must possess a documented activity relevant to cancer, along with evidence of mutations in cancer which change the activity of the gene product in a way that promotes oncogenic transformation. We also consider the existence of somatic mutation patterns across cancer samples gathered in COSMIC. For instance, tumour suppressor genes often show a broad range of inactivating mutations and dominant oncogenes usually demonstrate well defined hotspots of missense mutations. Genes involved in oncogenic fusions are included in Tier 1 when changes to their function caused by the fusion drives oncogenic transformation, or in cases when they provide regulatory elements to their partners (e.g. active promoter or dimerisation domain).
Tier 2
A new section of the Census, which consists of genes with strong indications of a role in cancer but with less extensive available evidence. These are generally more recent targets, where the body of evidence supporting their role is still emerging.
Hallmarks
New overviews of cancer gene function focused on hallmarks of cancer pull together manually curated information on the function of proteins coded by cancer genes and summarise the data in simple graphical form. They present a condensed overview of most relevant facts with quick access to the literature source, and define whether a gene has a stimulating or suppressive effect via individual cancer hallmarks. Genes with the hallmark descriptions available are marked with the hallmark icon, that when clicked, opens the hallmark page. Hallmark descriptions will be expanded to encompass more genes and updated on regular basis.
Cancer Gene Census
Show both tiers
Showing tier 1
Show tier 2
Show 25 entries
Export: CSV TSV Search:
Gene Symbol
Name
Entrez GeneId
Genome Location
Tier
Hallmark
Chr Band
Somatic
Germline
Tumour Types(Somatic)
Tumour Types(Germline)
Cancer Syndrome
ABI1
abl-interactor 1
10006
10:26746593-26860935
1
12.1
yes
AML

TCGA Label	Definition
ACC	Adrenocortical carcinoma
ALL	Acute lymphoblastic leukemia
BLCA	Bladder Urothelial Carcinoma
BRCA	Breast invasive carcinoma
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma
CLL	Chronic Lymphocytic Leukemia
COREAD	Colon adenocarcinoma and Rectum adenocarcinoma
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma
ESCA	Esophageal carcinoma
GBM	Glioblastoma multiforme
HNSC	Head and Neck squamous cell carcinoma
KIRC	Kidney renal clear cell carcinoma
LAML	Acute Myeloid Leukemia
LCML	Chronic Myelogenous Leukemia
LGG	Brain Lower Grade Glioma
LIHC	Liver hepatocellular carcinoma
LUAD	Lung adenocarcinoma
LUSC	Lung squamous cell carcinoma
MB	Medulloblastoma
MESO	Mesothelioma
MM	Multiple Myeloma
NB	Neuroblastoma
OV	Ovarian serous cystadenocarcinoma
PAAD	Pancreatic adenocarcinoma
PRAD	Prostate adenocarcinoma
SCLC	Small Cell Lung Cancer
SKCM	Skin Cutaneous Melanoma
STAD	Stomach adenocarcinoma
THCA	Thyroid carcinoma
UCEC	Uterine Corpus Endometrial Carcinoma

Drug-gene interactions

Cancer Feature: EGFR_mut

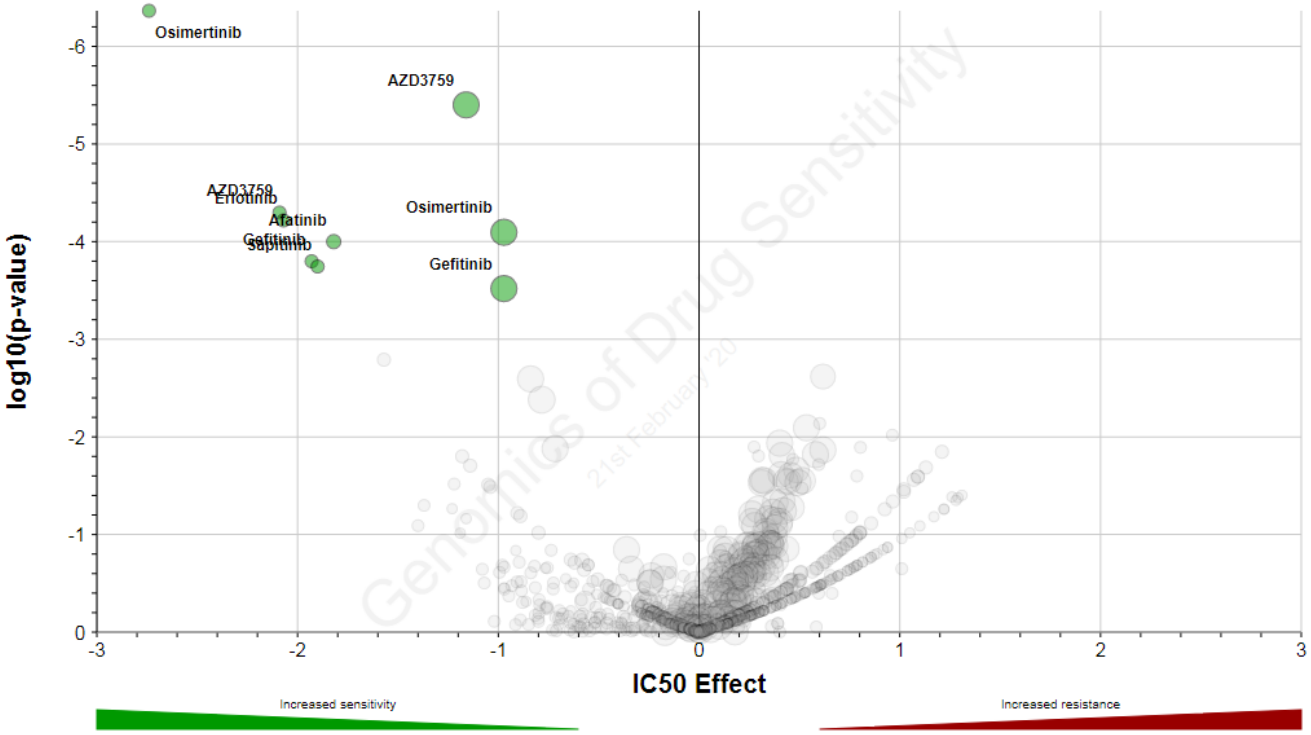
Dataset

- (•) GDSC2
- ( ) GDSC1

Volcano Plot | Scatter plots

Tissue analysis | Combined analysis

Associations from all tissue specific and pan-cancer ANOVA analyses overlaid. Hover the pointer over each circle to reveal the context-specific details of an association.



Drug	Drug Target	Effect size	P-value	FDR%	No. of altered cell lines	Tissue analysis
Osimertinib	EGFR	-2.74	4.32e-07	0.00129	5	LUAD
AZD3759	EGFR	-1.16	3.98e-06	0.264	20	PANCANCER
AZD3759	EGFR	-2.09	5.04e-05	0.101	5	LUAD
Erlotinib	EGFR	-2.07	6.07e-05	0.207	5	LUAD
Osimertinib	EGFR	-0.972	8.03e-05	1.78	20	PANCANCER
Afatinib	ERBB2, EGFR	-1.82	0.0001	0	6	LUAD
Gefitinib	EGFR	-1.93	0.000159	0.54	5	LUAD
Sapitinib	EGFR, ERBB2, ERBB3	-1.9	0.00018	0.647	5	LUAD
Gefitinib	EGFR	-0.972	0.000303	6.05	20	PANCANCER

Cancer Feature: MET_mut

Dataset

- (•) GDSC2
- ( ) GDSC1

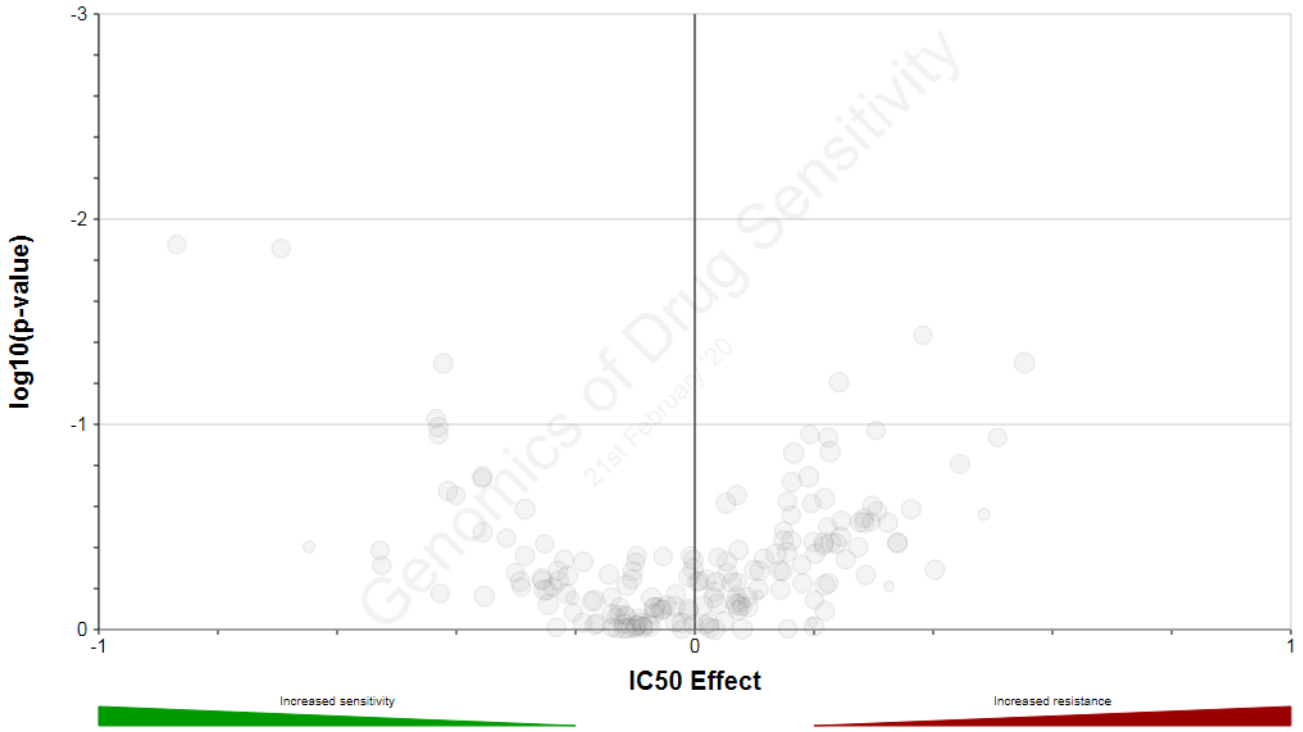
Tissue specific analysis

Pan-Cancer

Volcano Plot | Scatter plots

Tissue analysis | Combined analysis

Each circle represents an association between a genomic marker and drug sensitivity analysed using ANOVA. Different ANOVA analyses use selected context specific genomic markers as features. Use the dropdown to select a tissue specific analysis or a pan-cancer analysis.



Drug	Drug Target	Effect size	P-value	FDR%	No. of altered cell lines	Tissue analysis
Savolitinib	MET	-0.869	0.0133	46.7	10	PANCANCER
GNE-317	PI3Kalpha	-0.694	0.0139	28.9	10	PANCANCER
Ulixertinib	ERK1, ERK2	0.383	0.0368	82.8	10	PANCANCER
Camptothecin	TOP1	0.553	0.0501	63.4	12	PANCANCER
Olaparib	PARP1, PARP2	-0.422	0.0504	68.7	11	PANCANCER
Oxaliplatin	DNA alkylating agent	0.242	0.0623	32.4	11	PANCANCER
WEHI-539	BCL-XL	-0.434	0.0936	95.2	10	PANCANCER
LCL161	XIAP, IAP1, IAP2	-0.43	0.103	84.2	11	PANCANCER

Genomics of Drug Sensitivity in Cancer

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Compound: MK-2206

Drug Target: AKT1, AKT2

Drug Target pathway: PI3K/MTOR signaling

Dataset

- (•) GDSC2
- ( ) GDSC1

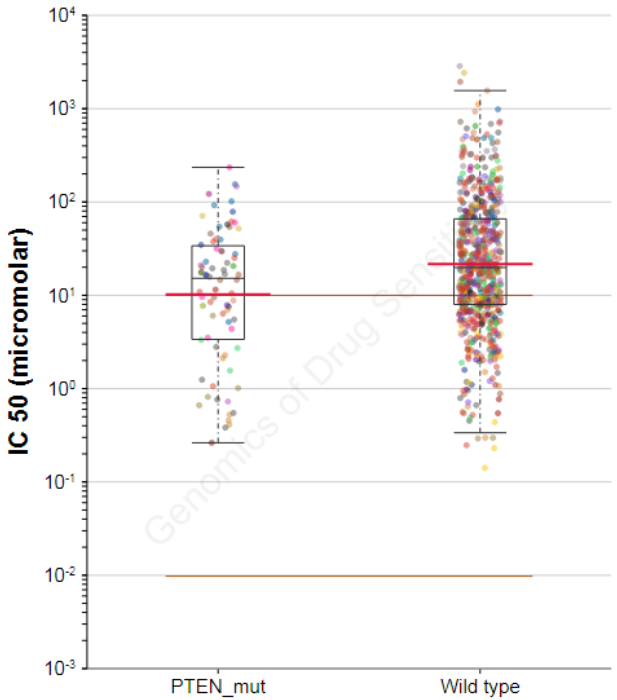
Tissue specific analysis

Pan-Cancer

Overview | IC50 by tissue | Volcano Plot | Scatter Plot | Compare compound

MK-2206 IC50 values for PTEN_mut

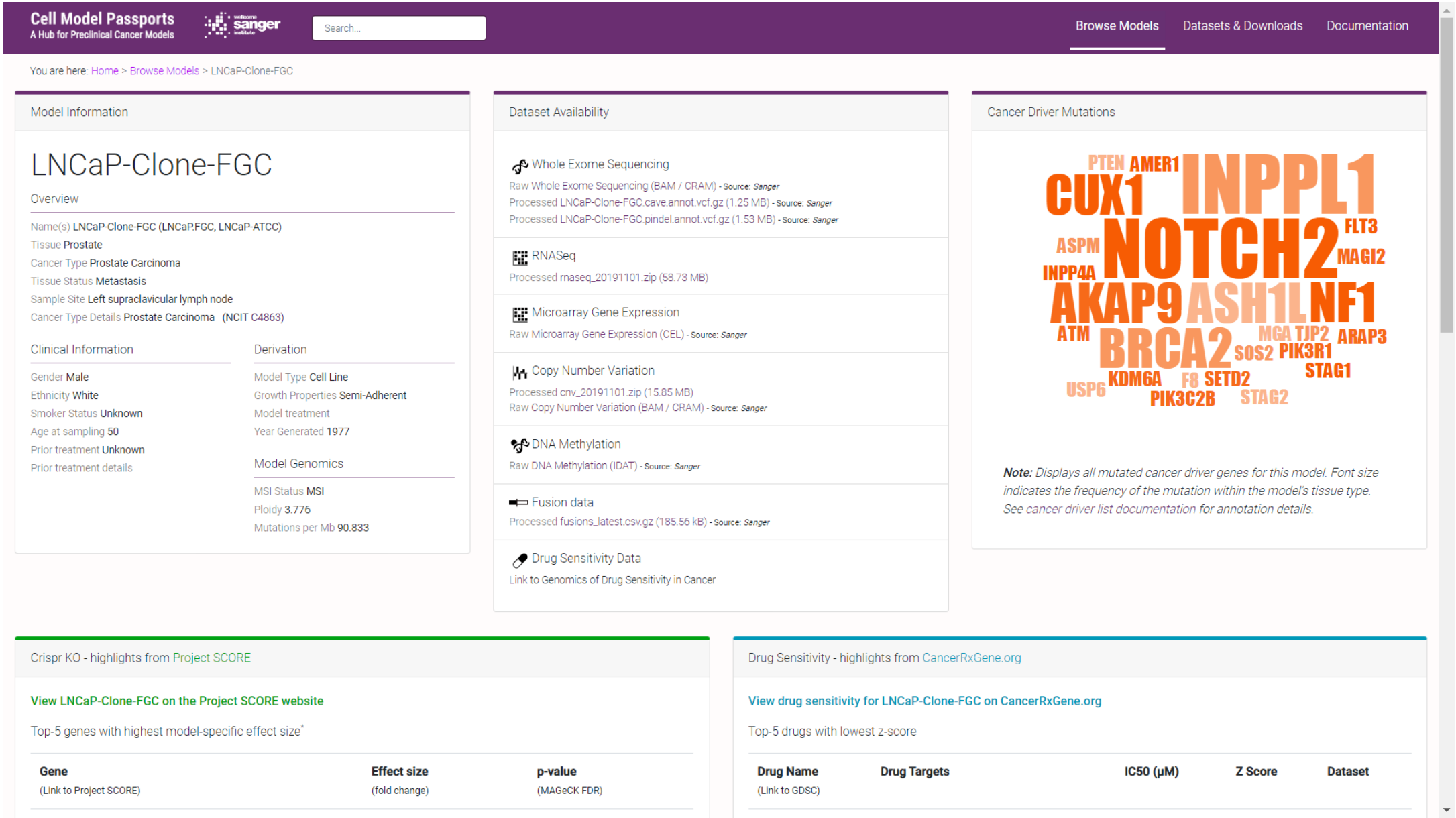
Click on circles to link to cell line information



Select Feature

Screening concentration: 0.0097656 (lower brown line) - 10.000 (upper brown line)

	PTEN_mut	Wild type	MWW p value	Signif	Selected
Number of cell lines	76	664			
Median	15.212	19.857			
Geometric mean (red line)	10.225	21.679			
Selected groups			0.00171	**	
ALL	6	18	0.049222	*	☑
ACC	0	1	-	-	☑
BLCA	1	17	1.0000	-	☑
BRCA	9	41	0.024614	*	☑
CESC	1	10	0.72727	-	☑
CLL	0	1	-	-	☑
COREAD	6	42	0.71996	-	☑
DLBC	4	14	0.15752	-	☑
ESCA	1	29	0.72888	-	☑
GBM	9	14	0.87486	-	☑
HNSC	2	24	0.59664	-	☑
KIRC	2	12	1.0000	-	☑
LIHC	1	14	0.66667	-	☑
LUAD	1	50	0.26230	-	☑
LUSC	0	15	-	-	☑
LCML	0	10	-	-	☑
LAML	1	16	1.0000	-	☑
LGG	2	7	0.66667	-	☑


Cell Model Passports
A Hub for Preclinical Cancer Models
sanger
Search...
Browse Models
Datasets & Downloads
Documentation
You are here: Home > Browse Models > LNCaP-Clone-FGC
Model Information
LNCaP-Clone-FGC
Overview
Name(s) LNCaP-Clone-FGC (LNCaP.FGC, LNCaP-ATCC)
Tissue Prostate
Cancer Type Prostate Carcinoma
Tissue Status Metastasis
Sample Site Left supraclavicular lymph node
Cancer Type Details Prostate Carcinoma (NCIT C4863)
Clinical Information
Gender Male
Ethnicity White
Smoker Status Unknown
Age at sampling 50
Prior treatment Unknown
Prior treatment details
Derivation
Model Type Cell Line
Growth Properties Semi-Adherent
Model treatment
Year Generated 1977
Model Genomics
MSI Status MSI
Ploidy 3.776
Mutations per Mb 90.833
Dataset Availability
Whole Exome Sequencing
Raw Whole Exome Sequencing (BAM / CRAM) - Source: Sanger
Processed LNCaP-Clone-FGC.cave.annot.vcf.gz (1.25 MB) - Source: Sanger
Processed LNCaP-Clone-FGC.pindel.annot.vcf.gz (1.53 MB) - Source: Sanger
RNASeq
Processed rnaseq_20191101.zip (58.73 MB)
Microarray Gene Expression
Raw Microarray Gene Expression (CEL) - Source: Sanger
Copy Number Variation
Processed cnv_20191101.zip (15.85 MB)
Raw Copy Number Variation (BAM / CRAM) - Source: Sanger
DNA Methylation
Raw DNA Methylation (IDAT) - Source: Sanger
Fusion data
Processed fusions_latest.csv.gz (185.56 kB) - Source: Sanger
Drug Sensitivity Data
Link to Genomics of Drug Sensitivity in Cancer
Cancer Driver Mutations
PTEN AMER1 CUX1 INPPL1 NOTCH2 FLT3 ASPM MAGI2 INPP4A AKAP9 ASH1L NF1 ATM BRCA2 MGA TJP2 ARAP3 SOS2 PIK3R1 STAG1 USP6 KDM6A F8 SETD2 PIK3C2B STAG2
Note: Displays all mutated cancer driver genes for this model. Font size indicates the frequency of the mutation within the model's tissue type. See cancer driver list documentation for annotation details.
Crispr KO - highlights from Project SCORE
View LNCaP-Clone-FGC on the Project SCORE website
Top-5 genes with highest model-specific effect size*
Gene (Link to Project SCORE)
Effect size (fold change)
p-value (MAGeCK FDR)
Drug Sensitivity - highlights from CancerRxGene.org
View drug sensitivity for LNCaP-Clone-FGC on CancerRxGene.org
Top-5 drugs with lowest z-score
Drug Name (Link to GDSC)
Drug Targets
IC50 (μM)
Z Score
Dataset

- https://score.depmap.sanger.ac.uk/
- https://depmap.sanger.ac.uk/
- **https://depmap.sanger.ac.uk/programmes/ (Drug response)**