

Corresponding author(s):	Shuang Zhao
Last updated by author(s):	7/20/2021

Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistics		
For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.		
n/a Confirmed		
The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement		
A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly		
The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.		
A description of all covariates tested		
A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons		
A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)		
For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted Give <i>P</i> values as exact values whenever suitable.		
For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings		
For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes		
\square Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated		
Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.		
Software and code		
Policy information about <u>availability of computer code</u>		
Data collection No software was used for data collection		
Data analysis R 3.4.4		

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data that support the findings of this study are available through the following locations. The Genomics of Drug Sensitivity in Cancer (GDSC) data were downloaded from the GDSC website (www.cancerrxgene.org). The Cancer Cell Line Encyclopedia (CCLE) dataset were downloaded from the CCLE website (portals.broadinstitute.org/ccle). The TCGA processed sequencing and clinical data were downloaded using the UCSC Xena browser (xena.ucsc.edu). The WCDT dataset with Whole Genome Sequencing and RNA-seq data is available at dbGAP (phs001648.v2.p1). Additional clinical data from the WCDT will be made upon request.

Field-specific reporting			
 		t is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.	
Life sciences		Behavioural & social sciences	
	 ∴he document w	ith all sections, see nature.com/documents/nr-reporting-summary-flat.pdf	
Life scier	nces s	tudy design	
All studies must dis	close on the	se points even when the disclosure is negative.	
Sample size	No sample s	size calculations were performed, as only previously published datasets were used.	
Data exclusions	No data excl	luded	
Replication	Not applicab	ple, one sample per patient was sequenced	
Randomization	Not applicab	ole	
Blinding	Not applicab	ple	
	6		
Reportin	g tor s	specific materials, systems and methods	
We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.			
Materials & experimental systems Methods			
n/a Involved in the study		n/a Involved in the study	
Antibodies			
Eukaryotic cell lines		— —	
MRI-based neuroimaging			
Animals and other organisms Repair of the control of the contr			
Clinical dat		ants	
Cillical dat	.d		
Human rese	arch par	ticipants	
Policy information about <u>studies involving human research participants</u>			
Population chara	cteristics	Men with metastatic castration-resistant prostate cancer	
Dogruitmont		Not applicable. Only previously published seherts were used	

Recruitment Not applicable. Only previously published cohorts were used. UCSF Institutional Review Board Ethics oversight

Note that full information on the approval of the study protocol must also be provided in the manuscript.