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# Highlights from the 1st European cancer dependency map symposium and workshop

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**The systematic identification of tumour vulnerabilities through perturbational experiments on cancer models, including genome editing and drug screens, is playing a crucial role in combating cancer. This collective effort is known as the *Cancer Dependency Map* (DepMap). The 1st European Cancer Dependency Map Symposium (EuroDepMap), held in Milan last May, featured talks, a roundtable discussion, and a poster session, showcasing the latest discoveries and future challenges related to the DepMap. The symposium aimed to facilitate interactions among participants across Europe, encourage idea exchange with leading experts, and present their work and future projects. Importantly, it sparked discussions on future endeavours, such as screening more complex cancer models and accounting for tumour evolution.**

**Keywords:** cancer; dependency map; large scale; screens; symposium; workshop; computational biology; CRISPR; cancer models; drug discovery

In his ancient Chinese treatise, *The Art of War*, the military strategist Sun Tzu emphasises the vital role of understanding the enemy to secure victory. Regarded as one of the most influential works on military strategy, Sun Tzu's anthology underscores the need to know the enemy's weaknesses, such as logistical vulnerabilities or internal divisions. These can be exploited to gain a decisive advantage on the battlefield. Sun Tzu's teachings resonate today, serving as a testament to the enduring wisdom of comprehending one's adversary in the pursuit of triumph.

Implementing this principle in cancer research is the initial stride towards crafting efficacious therapeutic strategies to combat cancer effectively. In this case, thoroughly knowing the enemy's weaknesses entails comprehensively exploring its genetic vulnerabilities and

**Abbreviations**
AML, acute myeloid leukaemia; CAFs, cancer-associated fibroblasts; CRISPR, Clustered Regularly Interspaced Short Palindromic Repeats; HT, Human Technopole; PDOs, inpatient-derived organoids; VUS, variants of unknown significance; WRN, Werner syndrome helicase.

dependencies across cells and tumour types. The *Cancer Dependency Map (DepMap)* represents a significant leap towards this goal: an ambitious project aiming to systematically identify and catalogue tumour vulnerabilities by performing perturbational experiments on cancer models via genome editing and drug screens [1,2].

With thousands of multi-omically characterised cancer cell lines and organoids already screened at the Wellcome Sanger and the Broad institutes (the two genome-research centres leading the effort, respectively in Cambridge (UK) and Cambridge (MA, USA)), and related databases made publicly accessible to the community through dedicated web tools and portals [3,4], DepMap is an unparalleled resource for systematically identifying new targets and markers for anti-cancer therapies [3,5–8], as well as exploring novel research avenues, conducting functional genetics studies [9] and elucidate the mode of action of existing drugs [10].

To provide a comprehensive overview of DepMap, along with the latest advancements in the application of chemogenomics and genome-editing screens for identifying new vulnerabilities in cancer and potential therapeutic targets, a group of scientists from the Human Technopole (HT) in Milan, Italy, the Wellcome Sanger Institute (WSI) and EMBL – European Bioinformatics Institute (EBI) both in Cambridge, UK, and the Swiss Federal Institute of Technology in Zürich (ETH) in Switzerland, have come together to organise the inaugural European Cancer Dependency Map Symposium (EuroDepMap).

This followed and was partially motivated by the call to action published in 2021 by researchers at WSI and Broad, some of whom were also organisers of EuroDepMap [2]. The call expressed a desire for a coordinated, collaborative initiative towards the creation of a comprehensive DepMap involving numerous research institutes, taking inspiration from previous large-scale projects in genomics like the Human Genome Project, 1000 Genomes, TCGA, ICGC, gnomAD, the Human Cell Atlas, and others. In this prospected grand endeavour, the EuroDepMap marked the crucial first step at the European level, setting the stage for future advancements and forging a path towards the realisation of this transformative goal.

## The 1st EuroDepMap in numbers

The 1st EuroDepMap was held in a hybrid in-presence/remote setting on May 8th 2023, at Human Technopole (HT): the new life science institute located in Italy at the core of the Milano Innovation District (MIND) and dedicated to advancing the fields of genomics, structural biology, neuroscience, computational, and data science and precision medicine to develop innovative solutions to some of the world's most pressing health challenges, including cancer.

HT aspires to achieve an essential objective while broadening its impact beyond the institute's boundaries: establishing a centre of excellence focused on nurturing and equipping junior researchers with advanced and interdisciplinary training encompassing various biomedical disciplines, methodologies, and state-of-the-art technologies. By doing so, HT aims to extend its activities to the broader community and foster a culture of excellence in research training. HT events are open to national and international researchers with a particular emphasis on catering to the needs and aspirations of early-career scientists.

In this framework, the 1st EuroDepMap was a successful example as (i) it created a unique platform for training and discussion on several disciplines and technologies that are sometimes perceived as 'single blocks' (i.e., computational biology, genomics, cancer, target therapy among others); (ii) it strongly attracted international and early-career scientists. Indeed, the event brought together around 200 individuals, including undergraduate and PhD students, postdoctoral fellows, research group leaders/professors, and industry representatives from 35 different nationalities. They were affiliated with research institutes, universities, and companies based in 24 countries. More than 50% of the attendees were junior researchers, specifically PhD/Master students and postdoctoral fellows. Gender representation was balanced overall by participants and among speakers, discussion panellists, and session chairs (Fig. 1).

Formal feedback received from participants after the event was overwhelmingly positive. An impressive 85% of participants reported acquiring a deeper understanding of the topic, demonstrating the event's success in imparting knowledge. Additionally, there was a unanimous consensus among participants suggesting that the event should be held regularly in the future.

## Covered topics, talks, and discussions

The 1st EuroDepMap provided an illuminating overview and served as a dynamic discussion forum, delving into a multitude of significant topics. These included: (i) The cutting-edge advancements and tireless efforts in the fields of cancer functional genomics and pharmacogenomics, with a focus on comprehensively identifying genetic dependencies and vulnerabilities across various types of human cancers; (ii) The growing prominence of systematic

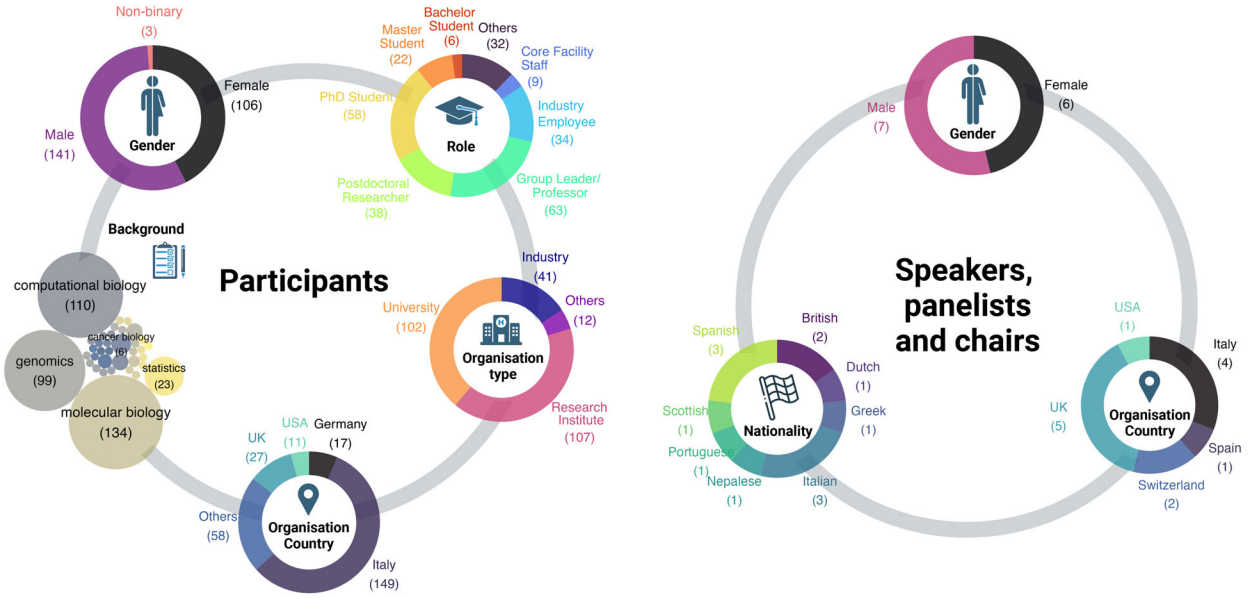


**Fig. 1.** Composition of participants and speakers/panellists/session-chairs of the first European Cancer Dependency Map Symposium.

perturbation experiments conducted on cancer pre-clinical models, showcasing how they play an increasingly pivotal role in unravelling the intricacies of cancer biology and therapeutic strategies; (iii) Thought-provoking discussions surrounding the current limitations of these experiments and the exciting prospects for future developments, aiming to enhance their efficiency, accuracy, and translatability; (iv) The remarkable strides made in sharing related data and results with the scientific community through dedicated web resources and portals, fostering collaboration and facilitating access to valuable information; (v) Insightful explorations of how the DepMap initiative has already made significant contributions to the field of oncology research, uncovering novel anti-cancer therapeutic targets and markers while supporting the realisation of the personalised medicine paradigm.

The above topics were presented in a number of talks delivered by high-profile speakers and experts in the fields. Participants were welcomed by an introductory speech by Iain Mattaj (the founding director of HT and formerly director of the European Molecular Biology Laboratory), who also declared: 'There is no doubt that some research is easier to justify to funders than others, so some efforts are easier choices. The Cancer DepMap is a concerted international attempt to use cancer genomic data and experimental findings, many of them generated in high-throughput analyses of cancer cells, to provide information that will help combat specific types of cancer in patients. It is a long-term project that requires large-scale research collaboration and strong interaction with both industries (pharma and biotech) and clinicians. As an institute Director, DepMap ticks all my favourite boxes. Such projects help to expand the horizons of everyone involved, to expand the networks of the younger researchers involved and to train everyone to think about problems from more than one perspective'.

Mathew Garnett and Paquita Vazquez, respectively from Wellcome Sanger and Broad Institutes, opened the talk series by discussing the origins of the DepMap. They reflected on the importance of seminal studies conducted in the 1990s, pioneered by the NCI-60 human tumour cell line screen [11], to systematically profile cell lines with compounds, and later studies using expanded panels of cell lines to encompass tumour heterogeneity [12]. They went on to mention milestones towards building a DepMap in the subsequent 10–15 years, including efforts to aggregate large panels of human cancer cell lines and their deep molecular annotation, large-scale systematic pharmacological screens to identify biomarkers of drug response [13,14], and the use of genetic perturbation, initially with RNAi, and most recently via clustered regularly interspaced short palindromic repeats (CRISPR) screens, to map genetic dependencies in cancer cell lines [1]. They explained how the analysis of DepMap datasets has required the development of a suite of computational tools [15–17] and the value of widely used public data portals such as the Genomics of Drug Sensitivity in Cancer [18], the Cell Model Passports [19], and DepMap portals [1,3,20,21], to enable their wider uptake and exploration of DepMap data.

Garnett and Vasquez went on to showcase the range of applications of the DepMap. This includes efforts to discover new targets, such as the Werner syndrome helicase (WRN) in microsatellite unstable colorectal cancers, which are in pre-clinical development [5,6], and drugs for targets such as PRMT5 in MTAP mutant cancers, which are now entering the clinic [22]. They highlighted the opportunity to generate new models for rare and paediatric cancer, where there is a large unmet clinical need, and to map their dependencies [23]. Furthermore, they showcased studies using co-essentiality analysis to describe novel gene function [9], integration of pharmacological and CRISPR data to understand drug mode of action [10], opportunities to identify drug combinations [24], to interpret cancer gene mutations and gene fusions [25], and to define human essential genes [26], amongst other possible applications.

They next reflected on the lessons learned so far. They emphasised the value of systematic data generation to encompass molecular diversity and to increase statistical power. They reflected on the need for proper data curation and the definition of standards to enable data integration. Furthermore, they thanked the generosity of their collaborators and emphasised the importance of interdisciplinary collaborations, given the potential scope and scale of the DepMap. They concluded their presentation by discussing opportunities to grow and expand the DepMap. These included, amongst others: (i) the ability to generate and perturb *in vitro* cellular models that better reflect the diversity of human cancers and their environmental niches, including stromal and immune cells, that impinge on tumour biology; (ii) the ability to increase the range of perturbations in cells using, for example, the expanding repertoire of genetic tools, tool compounds, or drug combinations. Additionally, they embraced the opportunity to apply a range of multi-modal readouts to cells and tissues at the genome, transcriptome and proteome levels to gain a deeper mechanistic understanding of cellular mechanisms and vulnerabilities. Lastly, they mentioned the prospective use of single-cell approaches, such as RNA sequencing and Cell Painting [27], to better understand the role of tumour heterogeneity and intracellular signalling in mediating cancer dependencies. Tracking the origins of the DepMap throughout the current day and beyond, this initial session brilliantly set the stage for the innovative work of the following speakers.

The morning session continued with a talk from Jolanda van Leeuwen, who presented her recent work on identifying context-dependent gene dependencies through genetic suppression analysis. Genes required for cellular viability are often highly conserved across eukaryotes. Still, in some cases, genomic 'suppressor' mutations have the potential to bypass their requirement, leading to context-dependent gene essentiality. Jolanda described recent work from her lab, in which they systematically studied differences in gene essentiality caused by spontaneous mutations [28], genetic backgrounds, and environments, using the budding yeast as a model system. She also illustrated how genetic variants can suppress the lethality of gene mutants in human cells, and how such interactions can drive tumour formation and chemotherapy resistance. The identified context-dependent essential genes showed considerable overlap between the two species and among the various genetic and environmental contexts with distinct properties conserved between yeast and humans [28]. Overall, Jolanda emphasised the importance of simple models to understand context-dependent genetic dependencies, and how the lessons learned from such studies can be used to predict dependencies in other contexts, including cancer.

Jolanda's talk was followed by a poster session that gave a chance to junior researchers to discuss their works with speakers and other experts. The poster session covered a wide range of topics related to cancer dependencies. Multiple projects focused on developing methods to correct artefacts and assess the technical quality of CRISPR-Cas9 screens while providing bioinformatic tools and web interfaces. Another widely discussed topic was the identification of molecular interactions at different levels to develop combinatorial treatments and patient stratification for precision medicine. Genetic interaction studies were also presented (e.g., paralogue interactions, context-specific synthetic lethality), focusing on determining altered proliferation rate or response to treatment such as radiotherapy. In addition, integrating multiple available omics on cancer cell lines was proposed to derive new knowledge. For instance, variants of unknown significance were explored in their relationship to cancer dependencies. Pooled genome-editing approaches were proposed in the context of the functional validation for central hubs in gene co-expression networks assembled for different breast cancer subtypes. Finally, some posters presented different CRISPR assays, such as base editing screenings to investigate mutagenesis of m6A-related genes, non-coding RNAs, and significant genes in acute myeloid leukaemia (AML).

The afternoon session started with a talk from Sumana Sharma from WIMM-University of Oxford. She presented CRISPR-based approaches to unravel the complex process of cellular signalling, ranging

from receptor identification to the inference of intracellular signalling pathways, emphasising signalling mediated by inhibitory immune checkpoints. Despite their wide use in cancer immunotherapy, Sumana pointed out that the signalling mechanism impinged by inhibitory immune checkpoints is still unclear. This implies that the potential advantages of these therapies may have yet to be fully capitalised. Therefore, Sumana proposed that future studies conducted by DepMap should incorporate immune components into cellular assays to enhance their effectiveness. She also demonstrated the power of CRISPR technology to identify regulators of signalling pathways [29,30], but emphasised the need to design appropriate cellular assays. Cancer cells often depend on dysregulated signalling pathways, so using large-scale screening approaches to untangle their mechanistic topology can be highly valuable.

Chris Tape from the UCL Cancer Institute gave a talk on single-cell analysis of drug response mechanisms inpatient-derived organoids (PDOs) and cancer-associated fibroblasts (CAFs), showing that CAFs alter PDO drug sensitivity by cell-fate plasticity switching and mechanistic insights can drive rational drug re-sensitisation [31]. Chris particularly emphasised that cell-extrinsic cues can regulate cancer cell dependencies and that future DepMap efforts would benefit from incorporating elements of the tumour microenvironment.

Finally, Nuria Lopez-Bigas from IRB presented her work on *in silico* saturation mutagenesis of cancer and clonal haematopoiesis genes. The fact that most mutations in cancer genes identified in tumours are variants of unknown significance (VUS) motivated her work. Nuria and her team devised an approach to automatically annotate driver versus passenger mutations in cancer genes, learning from observed mutations in thousands of tumours. Using machine learning models inspired by evolutionary biology, Nuria showed that the computational method BoostDM can effectively identify driver mutations in each gene and cancer type [32]. Applying trained models to all possible mutations in the genome, an *in silico* saturation mutagenesis can be achieved to outline blueprints of potential driver mutations in cancer genes. Nuria stressed the complementarity of these approaches with those currently implemented in the DepMap. In addition, she presented an extension of BoostDM modelling applied to clonal haematopoiesis. In this case, the machine learning approach underlying BoostDM is used on mutations observed in the blood of thousands of individuals to identify clonal haematopoiesis driver mutations effectively [33].

An open round-table discussion involving all the speakers and representatives from pharmaceutical companies, Peter Fenici from AstraZeneca and Laura Riva from Nerviano Medical Science, concluded the symposium. The discussion focused on critical aspects, emerging technologies, and both academic and industrial perspectives of DepMap. Laura and Peter emphasised the importance of DepMap, noting that it is regularly utilised by the groups focusing on oncology in their respective companies. They acknowledged the recent expansions of DepMap, now including combinatorial drug screens [24] and new data modalities like proteomic profiling [34]. However, they emphasised that future expansions of DepMap are necessary to address the currently limited representation of specific patient segments, genomic backgrounds, and ethnicities. Furthermore, they described DepMap as a 'gateway' to fostering collaborative solid research and facilitating the discovery of new therapeutics for diseases with high unmet needs. Lastly, they recognised the value of pre-competitive private-public partnerships, which bring together top-level scientists and cutting-edge technologies at the same 'virtual bench', facilitating the integration of academic research, drug discovery, and translational expertise.

## Future perspective

Following the symposium, a workshop brought together more than 20 renowned European researchers in cancer functional genomics and pharmacogenomics the next day. This event focused on the need for better integration of European efforts to collaborate on research on cancer dependencies. Throughout the scientific discussions held during the workshop, participants assessed the challenges and opportunities associated with embarking on such future endeavours.

Assessing cancer dependencies in more complex model systems better recapitulating the tumour immune microenvironment using rich, high dimensional readouts, such as single-cell RNAseq, was identified as a steppingstone towards identifying cancer cell-intrinsic dependencies as well as therapeutic opportunities to unleash the tumour-killing activity of the immune system. In addition, the community felt there is an opportunity to investigate dependencies along the entire spectrum of cancer evolution, from pre-cancer to metastatic disease. Such a strategy could open novel avenues to identify dependencies across the disease course, including early disease, where treatments are most likely to be successful.

In summary, EuroDepMap brought together a multidisciplinary group of scientists using perturbation technologies at scale to advance our ability to understand

mechanisms of cancer development and progression and to identify its vulnerabilities. The technologies and approaches presented include CRISPR screens at massive scales, multimodal read-outs, such as CyTOF or scRNAseq, using CRISPR to study signalling or context-specific essentiality and using the canvas of human population cancer genomics as a natural perturbation dataset. The diversity of viewpoints and approaches demonstrated, on the one hand, the power of perturbation technologies at scale, and on the other hand, the future opportunities and challenges that, as a community, we need to tackle to accomplish our mission. For example, the need for more read-outs at scale, diverse assays and more physiologically relevant model systems was discussed. The need to better capture the human population diversity at the genetic, gender, and ethnic background levels was also deemed essential to allow equitable access to care across all cancer patients.

In the future, it will also be important to couple worldwide efforts for the early detection of cancer and mechanisms of drug resistance by identifying vulnerabilities at different stages of cancer development.

The 1st EuroDepMap was a remarkable event that emphasised the active involvement of early-career scientists from academia, industry, and the clinical sector. It served as a unique platform that not only provided comprehensive training opportunities to gain insights into the current state of the field but also enabled participants to grasp the prospects and challenges lying ahead. However, its significance extended beyond knowledge acquisition alone. The event fostered a vibrant networking environment, allowing aspiring young scientists, driven by their shared interest in unravelling cancer dependencies, to forge meaningful connections that could shape their future careers in profound ways.

Undoubtedly, EuroDepMap was a resounding success, showcasing the remarkable strides already achieved through the Cancer Dependency Map projects. Yet, it also emphasised that this is merely the initial phase of a much larger journey. A tremendous amount of work remains to be undertaken, and international collaboration stands as an essential pillar in our collective battle against cancer. The workshop, which followed the symposium, assumes a pivotal foundational role for a future European Cancer Dependency Map Consortium, which will provide a forum to align and coordinate DepMap efforts across Europe and with other related initiatives.

EuroDepMap showcased the relentless progress in experimental and computational technologies, complemented by the unwavering diversity of approaches and the unbridled enthusiasm within the scientific community. As we look ahead, the future holds immense promise, positioning us to uncover the vulnerabilities of our 'enemy', and drawing inspiration from the teachings of Sun Tzu, leverage them to secure victory in our battle against cancer.

## Author contributions

All the authors were speakers, discussion panellists or organisers of the 1st European Cancer Dependency Map Symposium. All authors contributed to the manuscript writing. AS, LT and FI edited the manuscript. FI supervised symposium organisation and manuscript writing.

## References


1 Tsherniak A, Vazquez F, Montgomery PG, Weir BA, Kryukov G, Cowley GS, Gill S, Harrington WF, Pantel S, Krill-Burger JM *et al.* (2017) Defining a cancer dependency map. *Cell* **170**, 564–576.e16.

2 Boehm JS, Garnett MJ, Adams DJ, Francies HE, Golub TR, Hahn WC, Iorio F, McFarland JM, Parts L and Vazquez F (2021) Cancer research needs a better map. *Nature* **589**, 514–516.

3 Dwane L, Behan FM, Gonçalves E, Lightfoot H, Yang W, van der Meer D, Shepherd R, Pignatelli M, Iorio F and Garnett MJ (2021) Project score database: a resource for investigating cancer cell dependencies and prioritizing therapeutic targets. *Nucleic Acids Res* **49**, D1365–D1372.

4 Lenoir WF, Lim TL and Hart T (2018) PICKLES: the database of pooled *in-vitro* CRISPR knockout library essentiality screens. *Nucleic Acids Res* **46**, D776–D780.

5 Behan FM, Iorio F, Picco G, Gonçalves E, Beaver CM, Migliardi G, Santos R, Rao Y, Sassi F, Pinnelli M *et al.* (2019) Prioritization of cancer therapeutic targets using CRISPR-Cas9 screens. *Nature* **568**, 511–516.

6 Chan EM, Shibue T, McFarland JM, Gaeta B, Ghandi M, Dumont N, Gonzalez A, McPartlan JS, Li T, Zhang Y *et al.* (2019) WRN helicase is a synthetic lethal target in microsatellite unstable cancers. *Nature* **568**, 551–556.

7 Sharifnia T, Wawer MJ, Goodale A, Lee Y, Kazachkova M, Dempster JM, Muller S, Levy J, Freed DM, Sommer J *et al.* (2023) Mapping the landscape of genetic dependencies in chordoma. *Nat Commun* **14**, 1933.

8 Cervia LD, Shibue T, Borah AA, Gaeta B, He L, Leung L, Li N, Moyer SM, Shim BH, Dumont N *et al.* (2023) A ubiquitination Cascade regulating the integrated stress response and survival in carcinomas. *Cancer Discov* **13**, 766–795.

9 Lord CJ, Quinn N and Ryan CJ (2020) Integrative analysis of large-scale loss-of-function screens identifies robust cancer-associated genetic interactions. *Elife* **9**, e58925.

10 Gonçalves E, Segura-Cabrera A, Pacini C, Picco G, Behan FM, Jaaks P, Coker EA, van der Meer D, Barthorpe A, Lightfoot H *et al.* (2020) Drug mechanism-of-action discovery through the integration of pharmacological and CRISPR screens. *Mol Syst Biol* **16**, e9405.
11 Shoemaker RH (2006) The NCI60 human tumour cell line anticancer drug screen. *Nat Rev Cancer* **6**, 813–823.
12 McDermott U, Sharma SV, Dowell L, Greninger P, Montagut C, Lamb J, Archibald H, Raudales R, Tam A, Lee D *et al.* (2007) Identification of genotype-correlated sensitivity to selective kinase inhibitors by using high-throughput tumor cell line profiling. *Proc Natl Acad Sci USA* **104**, 19936–19941.
13 Barretina J, Caponigro G, Stransky N, Venkatesan K, Margolin AA, Kim S, Wilson CJ, Lehár J, Kryukov GV, Sonkin D *et al.* (2012) The cancer cell line encyclopedia enables predictive modelling of anticancer drug sensitivity. *Nature* **483**, 603–607.
14 Iorio F, Knijnenburg TA, Vis DJ, Bignell GR, Menden MP, Schubert M, Aben N, Gonçalves E, Barthorpe S, Lightfoot H *et al.* (2016) A landscape of pharmacogenomic interactions in cancer. *Cell* **166**, 740–754.
15 Iorio F, Behan FM, Gonçalves E, Bhosle SG, Chen E, Shepherd R, Beaver C, Ansari R, Pooley R, Wilkinson P *et al.* (2018) Unsupervised correction of gene-independent cell responses to CRISPR-Cas9 targeting. *BMC Genomics* **19**, 604.
16 Dempster JM, Boyle I, Vazquez F, Root DE, Boehm JS, Hahn WC, Tsherniak A and McFarland JM (2021) Chronos: a cell population dynamics model of CRISPR experiments that improves inference of gene fitness effects. *Genome Biol* **22**, 343.
17 Vinceti A, De Lucia RR, Cremaschi P, Perron U, Karakoc E, Mauri L, Fernandez C, Kluczynski KH, Anderson DS and Iorio F (2023) An interactive web application for processing, correcting, and visualizing genome-wide pooled CRISPR-Cas9 screens. *Cell Reports Methods* **3**, 100373.
18 Yang W, Soares J, Greninger P, Edelman EJ, Lightfoot H, Forbes S, Bindal N, Beare D, Smith JA, Richard Thompson I *et al.* (2012) Genomics of drug sensitivity in cancer (GDSC): a resource for therapeutic biomarker discovery in cancer cells. *Nucleic Acids Res* **41**, D955–D961.
19 van der Meer D, Barthorpe S, Yang W, Lightfoot H, Hall C, Gilbert J, Francies HE and Garnett MJ (2019) Cell model passports—a hub for clinical, genetic and functional datasets of preclinical cancer models. *Nucleic Acids Res* **47**, D923–D929.
20 Pacini C, Dempster JM, Boyle I, Gonçalves E, Najgebauer H, Karakoc E, van der Meer D, Barthorpe A, Lightfoot H, Jaaks P *et al.* (2021) Integrated cross-study datasets of genetic dependencies in cancer. *Nat Commun* **12**, 1661.
21 Dempster J, Pacini C, Pantel S, Behan F, Green T, Krill-Burger J, Beaver C, Younger S, Zhivich V, Najgebauer H *et al.* (2019) Agreement between two large pan-cancer genome-scale CRISPR knock-out datasets. *Nat Commun* **10**, 5817.
22 Kryukov GV, Wilson FH, Ruth JR, Paulk J, Tsherniak A, Marlow SE, Vazquez F, Weir BA, Fitzgerald ME, Tanaka M *et al.* (2016) MTAP deletion confers enhanced dependency on the PRMT5 arginine methyltransferase in cancer cells. *Science* **351**, 1214–1218.
23 Dharia NV, Kugener G, Guenther LM, Malone CF, Durbin AD, Hong AL, Howard TP, Bandopadhayay P, Wechsler CS, Fung I *et al.* (2021) A first-generation pediatric cancer dependency map. *Nat Genet* **53**, 529–538.
24 Jaaks P, Coker EA, Vis DJ, Edwards O, Carpenter EF, Leto SM, Dwane L, Sassi F, Lightfoot H, Barthorpe S *et al.* (2022) Effective drug combinations in breast, colon and pancreatic cancer cells. *Nature* **603**, 166–173.
25 Picco G, Chen ED, Alonso LG, Behan FM, Gonçalves E, Bignell G, Matchan A, Fu B, Banerjee R, Anderson E *et al.* (2019) Functional linkage of gene fusions to cancer cell fitness assessed by pharmacological and CRISPR-Cas9 screening. *Nat Commun* **10**, 2198.
26 Vinceti A, Karakoc E, Pacini C, Perron U, De Lucia RR, Garnett MJ and Iorio F (2021) CoRe: a robustly benchmarked R package for identifying core-fitness genes in genome-wide pooled CRISPR-Cas9 screens. *BMC Genomics* **22**, 828.
27 Willis C, Nyffeler J and Harrill J (2020) Phenotypic profiling of reference chemicals across biologically diverse cell types using the cell painting assay. *SLAS Discov* **25**, 755–769.
28 van Leeuwen J, Pons C, Tan G, Wang JZ, Hou J, Weile J, Gebbia M, Liang W, Shuteriqi E, Li Z *et al.* (2020) Systematic analysis of bypass suppression of essential genes. *Mol Syst Biol* **16**, e9828.
29 Sharma S and Petsalaki E (2018) Application of CRISPR-Cas9 based genome-wide screening approaches to study cellular Signalling mechanisms. *Int J Mol Sci* **19**, 933.
30 Sharma S, Dincer C, Weidemüller P, Wright GJ and Petsalaki E (2020) CEN-tools: an integrative platform to identify the contexts of essential genes. *Mol Syst Biol* **16**, e9698.
31 Zapatero MR, Tong A, Sufi J, Vlckova P, Rodriguez FC, Nattress C, Qin X, Hochhauser D, Krishnaswamy S and Tape CJ (2023) Trellis single-cell screening reveals stromal regulation of patient-derived organoid drug responses. *bioRxiv* doi: 10.1101/2022.10.19.512668
32 Muiños F, Martínez-Jiménez F, Pich O, Gonzalez-Perez A and Lopez-Bigas N (2021) *In silico* saturation mutagenesis of cancer genes. *Nature* **596**, 428–432.
33 Pich O, Reyes-Salazar I, Gonzalez-Perez A and Lopez-Bigas N (2022) Discovering the drivers of clonal hematopoiesis. *Nat Commun* **13**, 4267.
34 Gonçalves E, Poulos RC, Cai Z, Barthorpe S, Manda SS, Lucas N, Beck A, Bucio-Noble D, Dausmann M, Hall C *et al.* (2022) Pan-cancer proteomic map of 949 human cell lines. *Cancer Cell* **40**, 835–849.e8.