

Supplementary information

Supplementary Fig. 1. Boxplot and Bipartite.

Supplementary Fig. 2. Knockdown efficiency of *CDKN2A* was determined by Western blot.

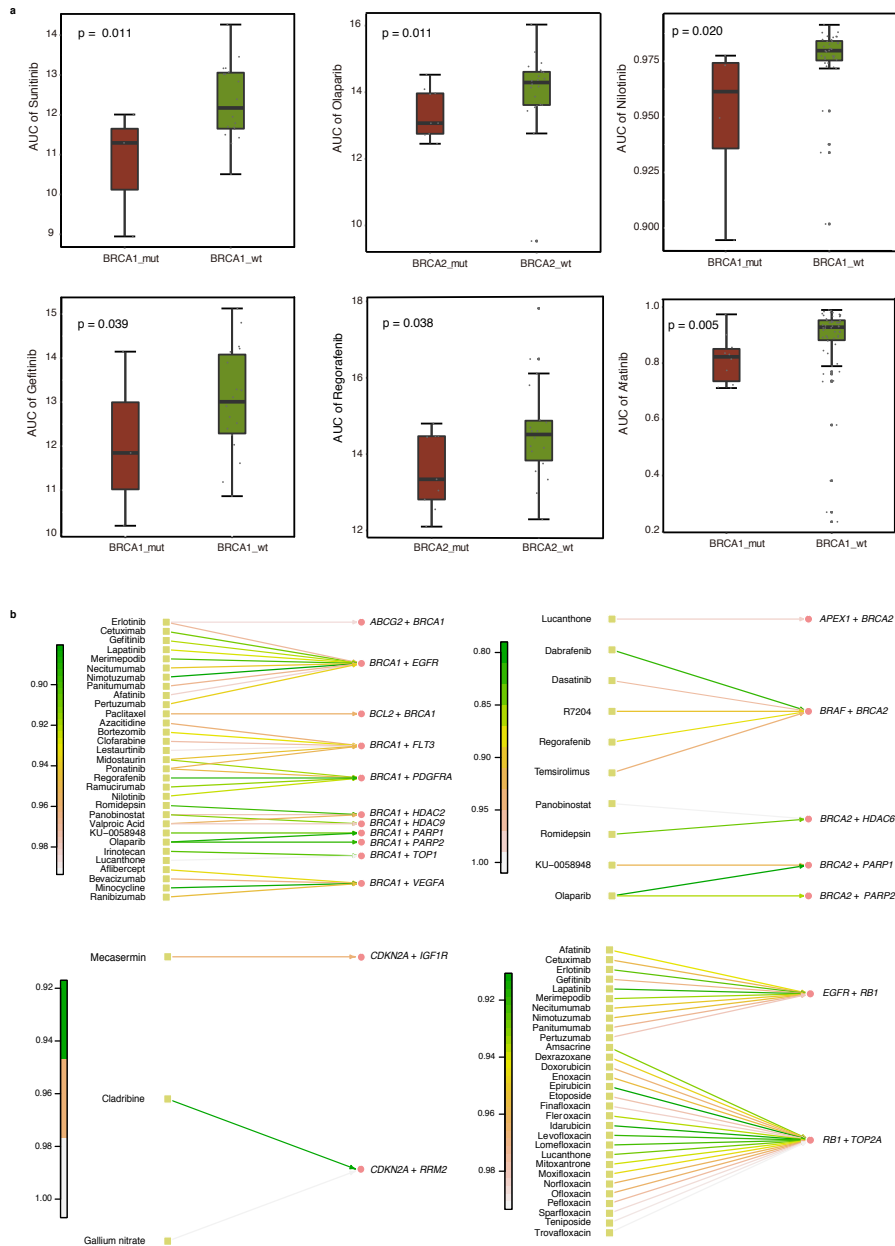
Supplementary Table 1. Literature supports for the top 20 repurposable drug candidates.

Supplementary Table 2. Clinical trial records of the top repurposable drug candidates based on SL and SDL respectively.

Supplementary Table 3. Best repurposable drug candidates of SL and SDL.

Supplementary Table 4. Mapping between tumors and cancer types.

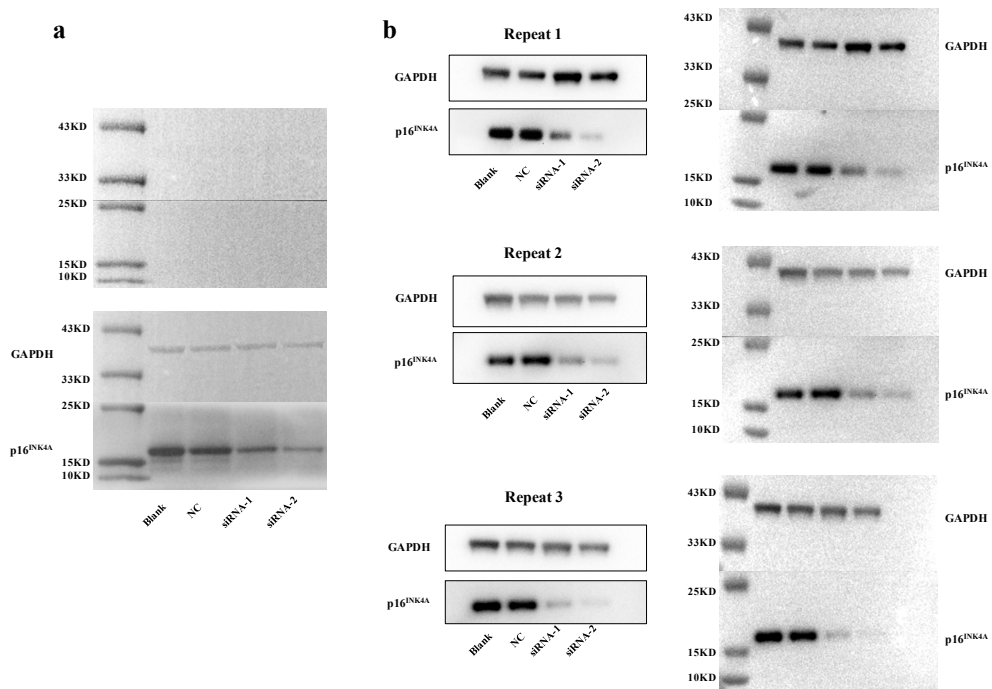
Supplementary Table 5. Primer sequences used in this study.



Supplementary Fig. 1. Boxplot and Bipartite.

a, Boxplot of one-sided Wilcoxon rank sum test based on SL (AUC). Box plots indicate median (middle line), 25th, 75th percentile (box) and 5th and 95th percentile (whiskers) as well as outliers (single points), $n = 42$ independent experiments in AUC of Sunitinib, $n = 31$ independent experiments in AUC of Olaparib, $n = 40$ independent experiments in AUC of Nilotinib, $n = 84$ independent experiments in AUC of Gefitinib, $n = 27$ independent experiments in AUC of Regorafenib, $n = 64$ independent experiments in AUC of Afatinib; Dots represent cancer cell lines.

b, Bipartite graph between drug (yellow square) and SL pairs (pink circle). Side annotation bar represents DrugScore.



Supplementary Fig. 2. Knockdown efficiency of *CDKN2A* was determined by Western blot.

a. Full scans of figure 6(b).

b. Knockdown efficiency of *CDKN2A* was repeated at 3 times independently with similar results.

Supplementary Table 1: Supported drug repositioning results by literatures(Top 20)

Type	Rank	Drug	Known Indications	Repositioning of the Cancer	Target Gene	GeneA+GeneB	MutationGene	Score
SL	3	Rucaparib	Breast cancer	Hereditary Breast and Ovarian Cancer Syndrome	PARP1	BRCA1 + PARP1	BRCA1	0.913
SL	4	Rucaparib	Breast cancer	Hereditary Breast and Ovarian Cancer Syndrome	PARP1	BRCA2 + PARP1	BRCA2	0.894
SL	14	Romidepsin	Peripheral T-cell lymphoma	Hereditary Breast and Ovarian Cancer Syndrome	HDAC2	BRCA1 + HDAC2	BRCA1	0.648
SL	17	Erlotinib	Colon cancer; Glioma; Breast cancer; Head and neck cancer	Retinoblastoma	EGFR	EGFR + RB1	RB1	0.607
SL	18	Erlotinib	Pancreatic cancer	Hereditary Breast and Ovarian Cancer Syndrome	EGFR	BRCA1 + EGFR	BRCA1	0.583
SL	20	Rucaparib	Ovarian cancer	Hereditary Breast and Ovarian Cancer Syndrome	PARP2	BRCA2 + PARP2	BRCA2	0.564
SDL	6	Vandetanib	Solid tumours	Carcinoma, Pancreatic Ductal	EGFR	EGFR + NOTCH1	NOTCH1	0.687
SDL	20	Lapatinib	Breast cancer	Carcinoma, Pancreatic Ductal	EGFR	EGFR + NOTCH1	NOTCH1	0.428

Literatures:

- 1 D. C. Pearre and K. S. Tewari, "Targeted treatment of advanced ovarian cancer: Spotlight on rucaparib," *Ther. Clin. Risk Manag.*, vol. 14, pp. 2189–2201, 2018
- 2 D. Pchejetski, A. Alfraidi, K. Sacco, H. Alshaker, A. Muhammad, and L. Monzon, "Histone deacetylases as new therapy targets for platinum-resistant epithelial ovarian cancer," *J. Cancer Res. Clin. Oncol.*, vol. 142, no. 8, pp. 1659–1671, 2016
- 3 Y. Shao et al., "Erlotinib has tumor inhibitory effect in human retinoblastoma cells," *Biomed. Pharmacother.*, vol. 85, pp. 479–485, 2017.
- 4 K. Nakai, M. C. Hung, and H. Yamaguchi, "A perspective on anti-EGFR therapies targeting triple-negative breast cancer," *Am. J. Cancer Res.*, vol. 6, no. 8, pp. 1609–1623, 2016.
- 5 A. Turk and K. B. Wisinski, "PARP Inhibition in BRCA-Mutant Breast Cancer," *Cancer*, vol. 124, no. 12, p. 2498, 2018.
- 6 A. D. Singhi et al., "Real-Time Targeted Genome Profile Analysis of Pancreatic Ductal Adenocarcinomas Identifies Genetic Alterations That Might Be Targeted With Existing Drugs or Used as Biomarkers," *Gastroenterology*, vol. 156, no. 8, pp. 2242–2253.e4, 2019.
- 7 N. Walsh et al., "EGFR and HER2 inhibition in pancreatic cancer," *Invest New Drugs*, vol. 31, pp. 558–566, 2013.

Supplementary Table 2: Clinical trial records of the top repurposable drug candidates based on SL and SDL

Class	Drug	Repositioning of cancer	Clinical trial title
SL	Olaparib	Hereditary Breast and Ovarian Cancer Syndrome	Palbociclib With Cetuximab and IMRT for Locally Advanced Squamous Cell Carcinoma
SL	Cetuximab	Retinoblastoma	Study of Treatment for Patients With Cancer of the Eye -Retinoblastoma
SL	Gefitinib	Retinoblastoma	PErsonalized TREATment of High-risk MAMmary Cancer - the PETREMAC Trial
SL	Lapatinib	Retinoblastoma	Vincristine, Carboplatin, and Etoposide or Observation Only in Treating Patients Who Have Undergone Surgery for Newly Diagnosed Retinoblastoma
SL	Paclitaxel	Hereditary Breast and Ovarian Cancer Syndrome	Molecular Phenotype Changes and Personalized Treatment for CRPC
SL	Pertuzumab	Retinoblastoma	Molecular Phenotype Changes and Personalized Treatment for CRPC
SL	Temsirolimus	Hereditary Breast and Ovarian Cancer Syndrome	-PATROL - Non-interventional Study (NIS) to Collect Clinical and Patient Reported Outcome Data in an Olaparib Treated BRCA ⁺ PSR Ovarian Cancer Population
SL	Epirubicin	Retinoblastoma	Veliparib, Carboplatin, and Paclitaxel in Treating Patients With Advanced Solid Cancer
SL	Etoposide	Retinoblastoma	Anastrozole, Palbociclib, Trastuzumab and Pertuzumab in Her-positive, Her2-positive Metastatic Breast
SL	Doxorubicin	Retinoblastoma	Temsirolimus and Vinorelbine Ditartrate in Treating Patients With Unresectable or Metastatic Solid Tumors
SDL	Vandetanib	Lymphoma	Testing Afatinib as a Potential Targeted Treatment in Cancers With HER2 Genetic Changes (MATCH-Subprotocol B)
SDL	Afatinib	Lymphoma	Serial Measurements of Molecular and Architectural Responses to Therapy (SMMART) PRIME Trial
SDL	Cetuximab	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma	Safety, Tolerability, Pharmacokinetics and Preliminary Efficacy of SCT200 in Patients With Advanced Solid Tumors
SDL	Afatinib	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma	CD19 CAR-T Cells for Patients With Relapse and Refractory CD19+ B-ALL.
SDL	Panitumumab	Lymphoma	A Phase 1 Dose-Escalation Study in Advanced Solid Tumors, Lymphomas or Multiple Myeloma
SDL	Lidocaine	Lymphoma	Serial Measurements of Molecular and Architectural Responses to Therapy (SMMART) PRIME Trial
SDL	Cetuximab	Lymphoma	A Study of LY2875358 in Japanese Participants With Advanced Cancer
SDL	Erlotinib	Lymphoma	S0528 Lapatinib and Everolimus in Treating Patients With Advanced Solid Tumors or Non-Hodgkin's Lymphoma
SDL	Erlotinib	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma	Recalcitrant Pruritus in Cutaneous T-Cell Lymphoma
SDL	Gefitinib	Lymphoma	REAL3 Trial of Efficacy of EOX With/Without Panitumumab in Previously Untreated Adv OG Cancer
SDL	Lapatinib	Lymphoma	ted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)
SDL	Pertuzumab	Lymphoma	Serial Measurements of Molecular and Architectural Responses to Therapy (SMMART) PRIME Trial
SDL	Vandetanib	Leukemia	Vandetanib and Bevacizumab in Treating Patients With Advanced Solid Tumors or Lymphoma
SDL	Pertuzumab	Precursor T-Cell Lymphoblastic Leukemia-Lymphoma	Vandetanib and Bevacizumab in Treating Patients With Advanced Solid Tumors or Lymphoma

Supplementary Table 4: Mapping between tumors and cancer types

Repositioning of the Cancer	Cancer Type	Cancer Type Name
Familial medullary thyroid carcinoma	THCA	Thyroid carcinoma
Hereditary Breast and Ovarian Cancer Syndrome	BRCA;OV	Breast invasive carcinoma;Ovarian serous cystadenocarcinoma
Ovarian Carcinoma	OV	Ovarian serous cystadenocarcinoma
Melanoma-Pancreatic Cancer Syndrome	SKCM;PAAD	Skin Cutaneous Melanoma;Pancreatic adenocarcinoma
Small cell carcinoma of lung	LUAD	Lung adenocarcinoma
Carcinoma,Pancreatic Ductal	PAAD	Pancreatic adenocarcinoma
Leukemia, T-Cell	LAML	Acute Myeloid Leukemia
Lymphoma	NULL	NULL
Precursor T-Cell Lymphoblastic Leukemia-	LAML	Acute Myeloid Leukemia
Lymphoma	NULL	NULL
Retinoblastma	NULL	NULL

Supplementary Table 5. Primer sequences used in this study

Gene	Sequence
CDKN2A-Forward	TCTGGAGTGAGCACTCACGC
CDKN2A-Reverse	GCTTGTCATGAAGTCGACAGCTTT
GAPDH1-Forward	ATGACATCAAGAAGGTGGTG
GAPDH1-Reverse	CATACCAGGAAATGAGCTTG