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Supplemental information

Personalized drug screening in patient-derived organoids of biliary tract cancer and its clinical application

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Fig.S1

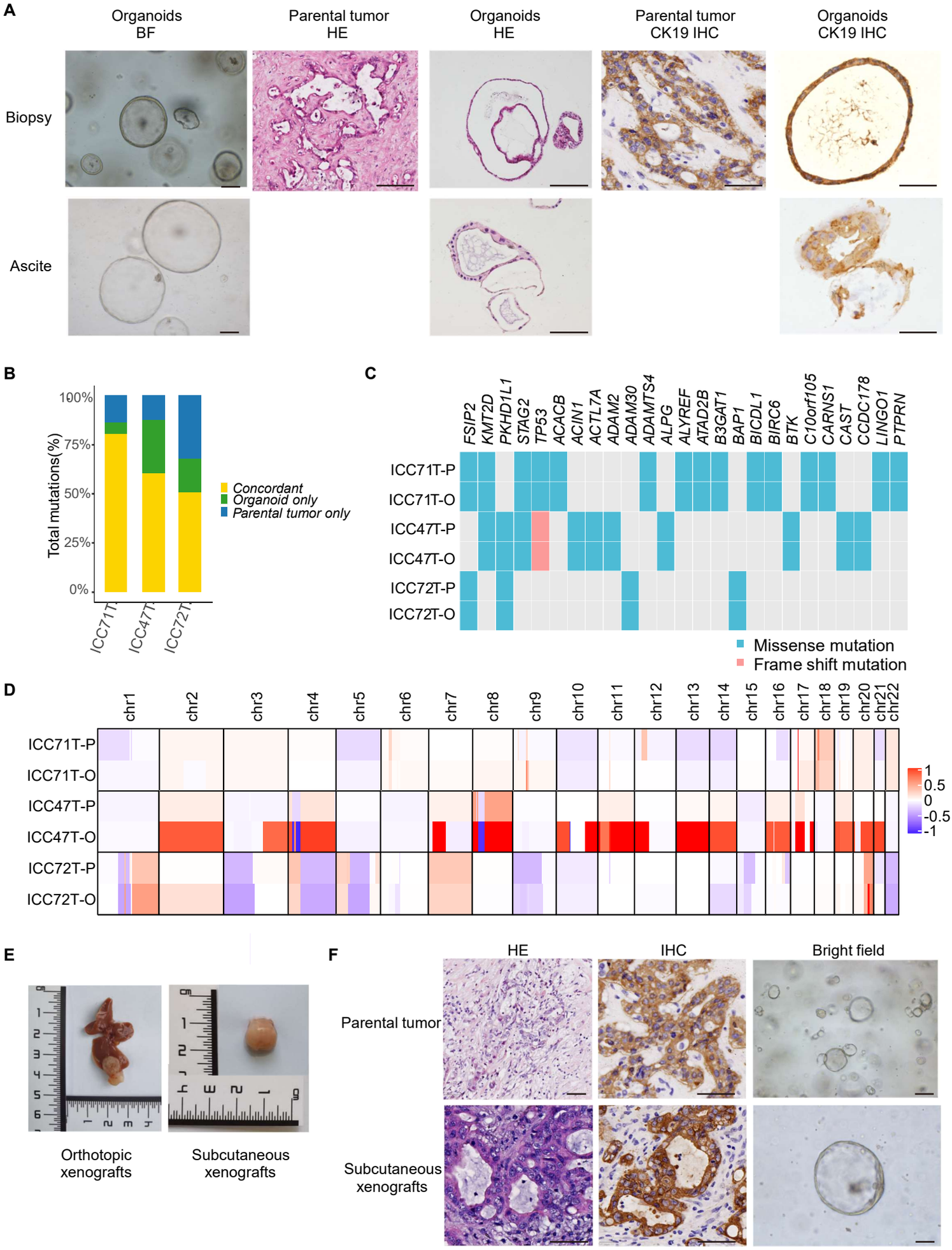


Figure S1. Patient-derived organoids established for the BTC biobank, related to Figure 1. (**A**) Representative bright field, HE and IHC microscopy images of patient-derived BTC organoids and matched primary tumors from biopsy and ascite. Scale bars, 50μm. (**B**) Concordance of mutations detected in the parental tumor and corresponding organoid lines. (**C**) Recurrent mutations identified in the parental tumor and corresponding organoid lines by WES. Displayed are the top 20 mutated genes observed in the data. P, parental tumor tissue; O, organoid. (**D**) Copy-number analyses in representative matched primary tumor specimens and corresponding PDOs. (**E**) Representative images of orthotopic tumor xenografts and subcutaneous tumor xenografts produced by patient-derived BTC organoids. (**F**) Representative HE, IHC and bright field microscopy images of patient-derived BTC organoids xenografts. Scale bars, 50μm.

Fig.S2

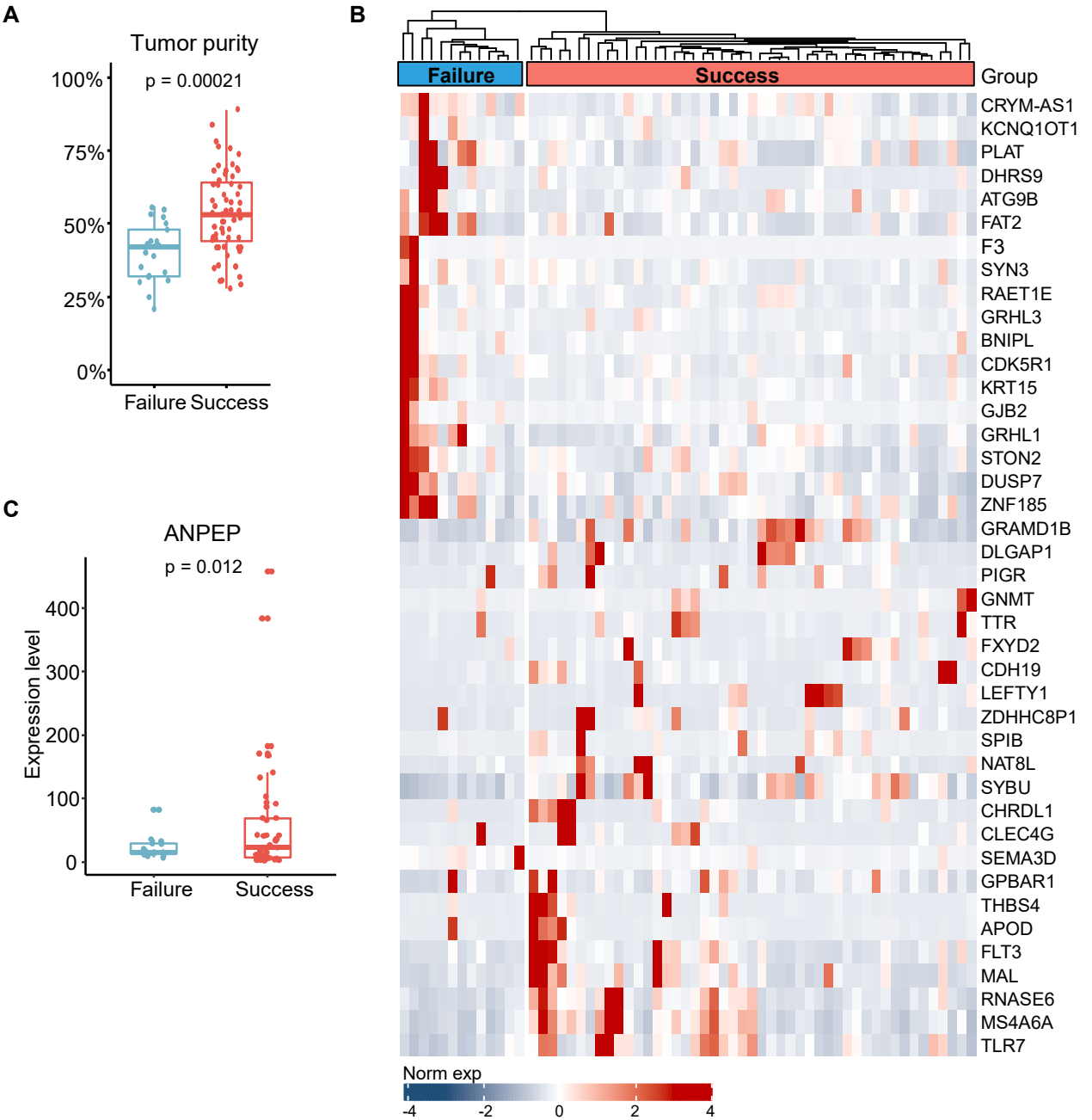


Figure S2. Stemness markers of the successful organoid culture tissues, related to Figure 2. (**A**) The tumor purity of successful organoid culture tissues and failed organoid culture tissues evaluated by H&E staining. Wilcoxon Rank Sum test. (**B**) The expression levels of differentially expressed genes between the successful and failed organoid culture tissues. (**C**) The expression level of ANPEP between successful organoid culture tissues and failed organoid culture tissues. Wilcoxon Rank Sum test.

Fig.S3

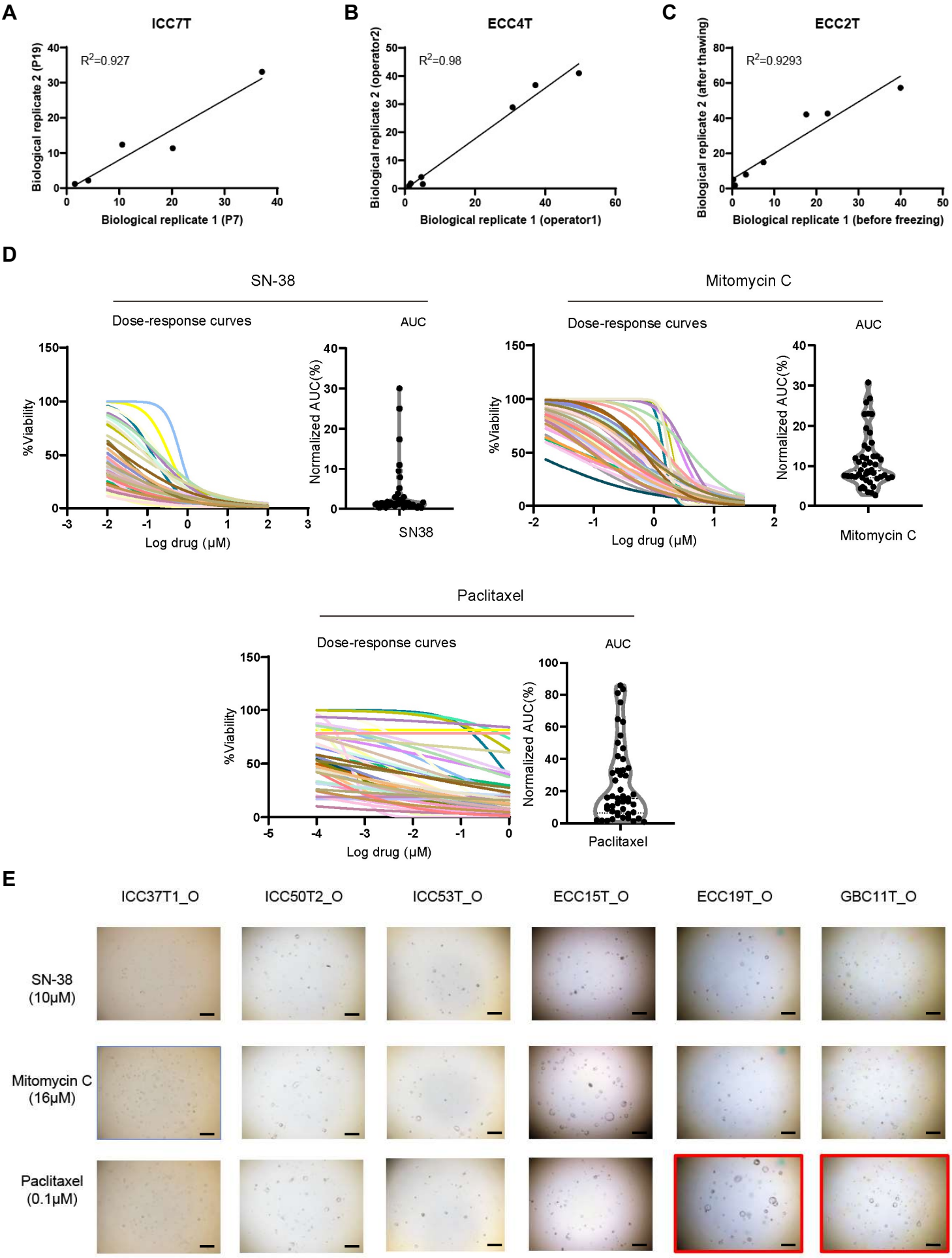


Figure S3. Stability responses of BTC organoids to chemotherapy *ex vivo*, related to Figure 3. (**A**) Concordance among viability readings obtained from organoids in different generation (n=3). (**B**) Concordance among viability readings obtained by different operators (n=3). (**C**) Concordance among viability readings obtained before freezing and after thawing (n=3). (**D**) *Ex vivo* chemosensitivity of 47 BTC organoids to SN-38, Mitomycin C and Paclitaxel in the form of dose response curves are displayed for each organoid (n=3). AUC was calculated from the raw dose–response data and is displayed as a violin plot; Colored data points indicate 47 BTC organoids respectively. (**E**) Effects on the viability of SN-38, Mitomycin C and Paclitaxel using an organoid-formation assay. Red square, resistant; no square, no viable cells. Scale bar, 100 μm.

Fig.S4

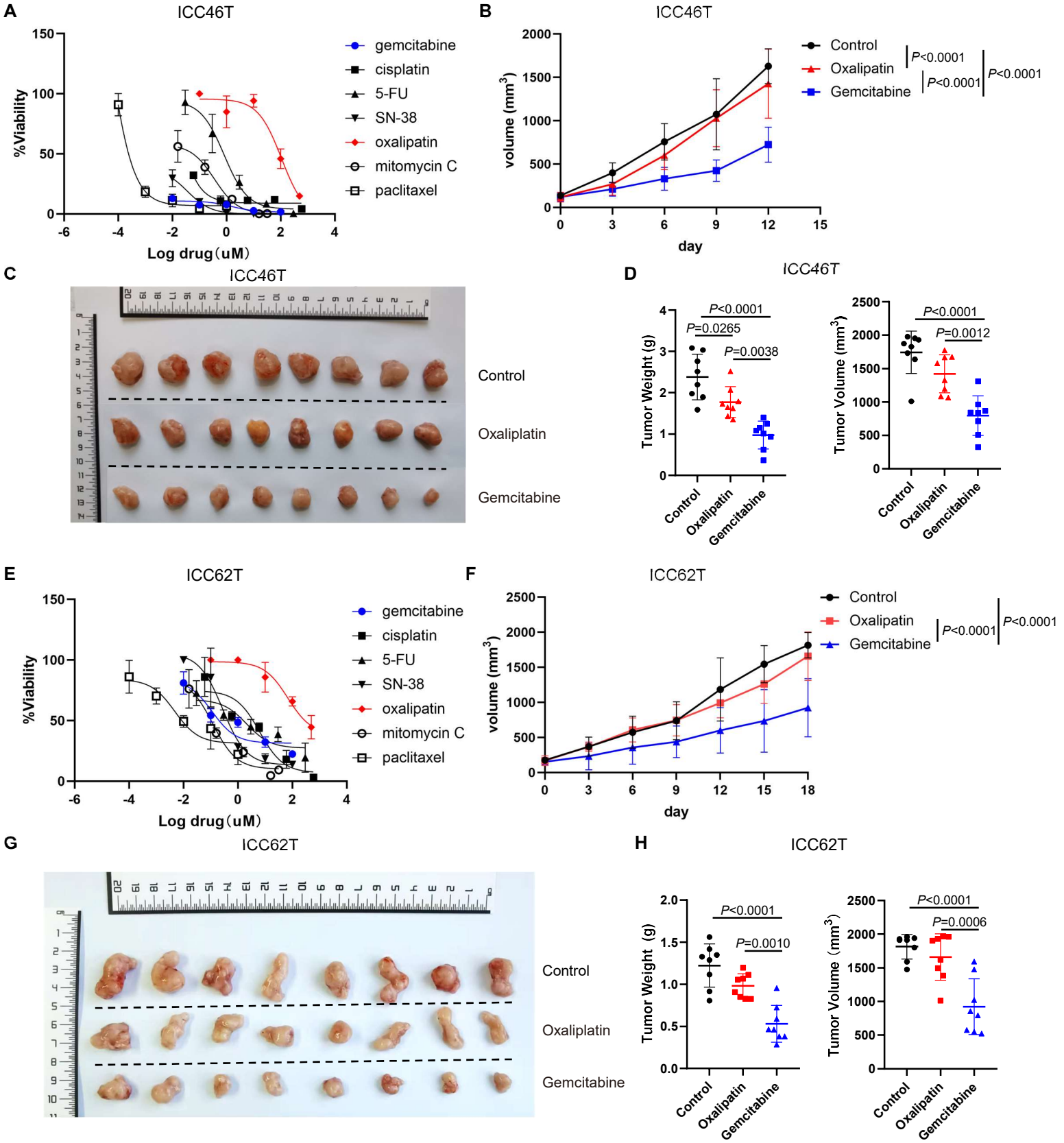


Figure S4. Consistent clinical responses to chemotherapy in other BTC organoids *in vivo*, related to Figure 4. (**A**) Dose-response curves of ICC46 organoid treated with the chemotherapeutic drugs, as measured using the Cell Titer-Glo cell viability assay (n=3). (**B**) Growth curves of ICC46 organoid subcutaneous xenografts in NCG mice. Mice were treated with Oxaliplatin, Gemcitabine or vehicle twice/week for 12 days (n=8). Results are shown as the tumor volume. (**C**) A representative image of tumor xenografts harvested 12 days after treatment with Oxaliplatin, Gemcitabine or vehicle (n=8). (**D**) The tumor weight and volume of the drugs/vehicle mice at the experimental end point (n=8). (**E**) Dose-response curves of ICC62 organoid treated with the chemotherapeutic drugs, as measured using the Cell Titer-Glo cell viability assay (n=3). (**F**) Growth curves of ICC62 organoid subcutaneous xenografts in NCG mice. Mice were treated with Oxaliplatin, Gemcitabine or vehicle twice/week for 18 days (n=8). Results are shown as the tumor volume. (**G**) A representative image of tumor xenografts harvested 18 days after treatment with Oxaliplatin, Gemcitabine or vehicle (n=8). (**H**) The tumor weight and volume of the drugs/vehicle mice at the experimental end point (n=8).

Fig.S5

A

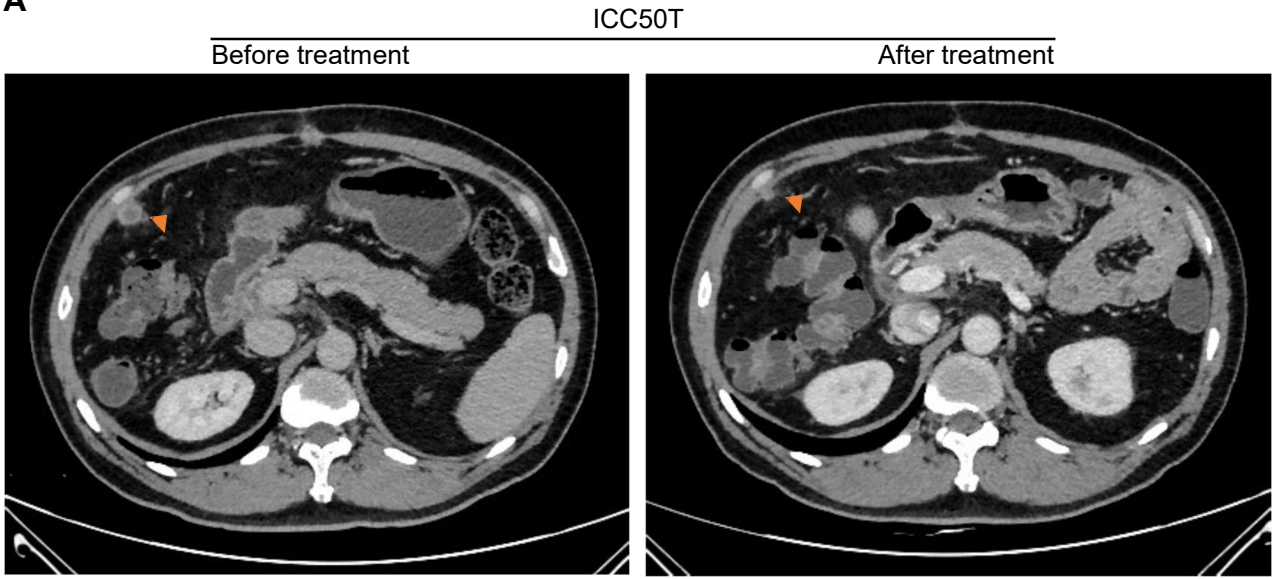


Figure S5. Comparison of drug response between patients on drug treatment and their corresponding cancer organoids, related to Figure 5. (**A**) CT scan of patient ICC50T before and 3 months after treatment with gemcitabine plus oxaliplatin. The nodule of abdominal wall showed shrinkage in size.

FigS6

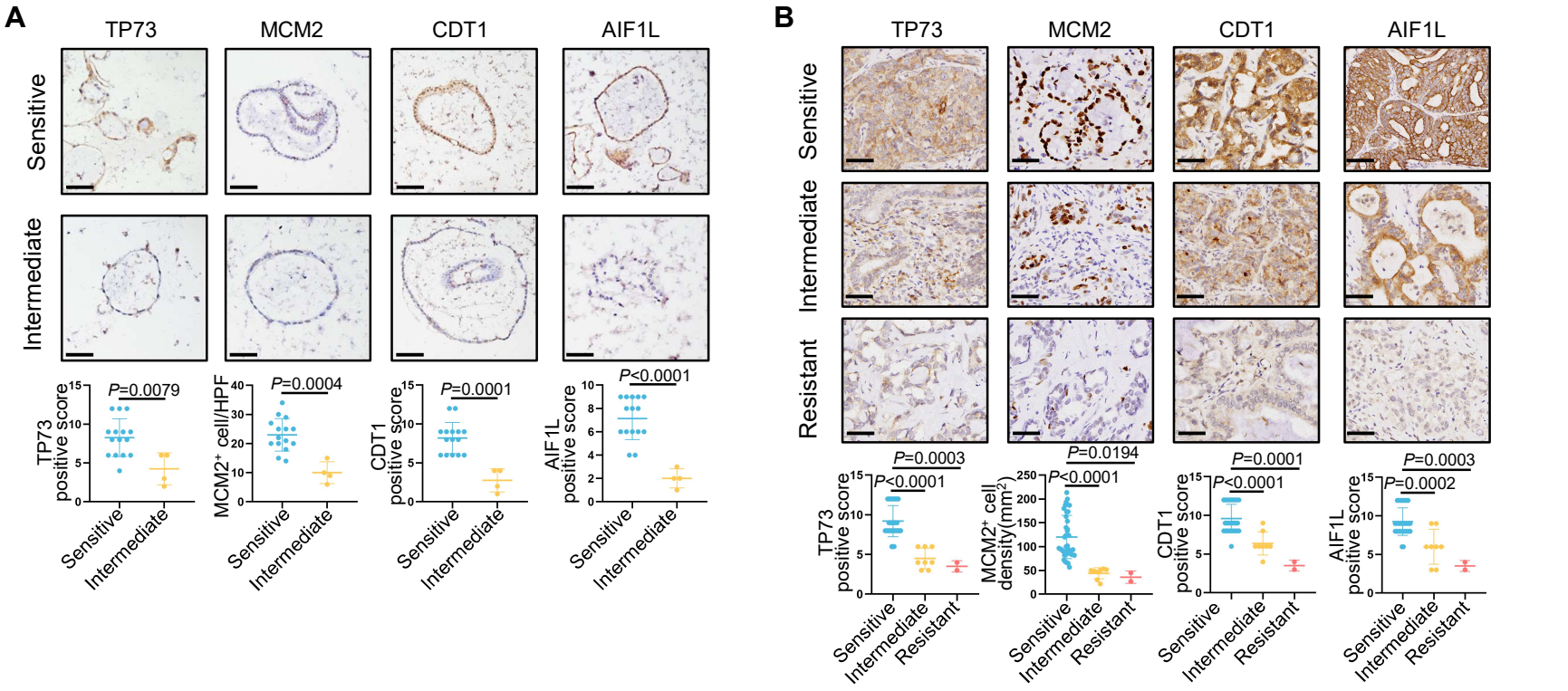


Figure S6. Transcriptional characteristics of 5-FU-sensitive group, related to Figure 6. (**A**) Immunohistochemical staining of 5-FU-sensitive markers in the derived organoids. Quantification of staining intensities for the indicated markers performed in 19 organoid samples. Scale bars, 20 μm. (**B**) Immunohistochemical staining of 5-FU-snesitive markers in tumor specimens of the whole cohort. Quantification of staining intensities for the indicated markers performed in 45 BTC tissue samples. Scale bars, 50 μm.

Fig.S7

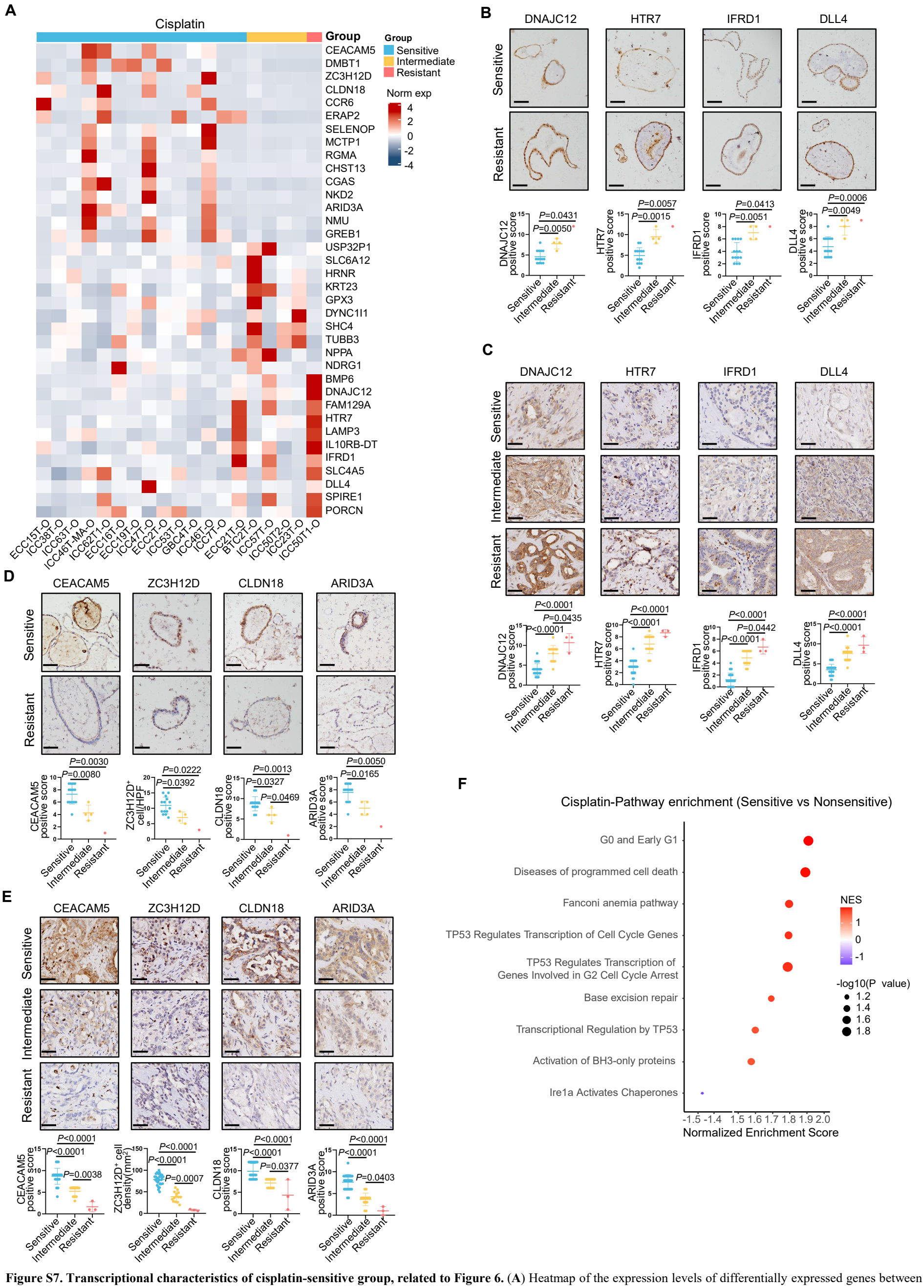


Figure S7. Transcriptional characteristics of cisplatin-sensitive group, related to Figure 6. (**A**) Heatmap of the expression levels of differentially expressed genes between cisplatin-sensitive group, cisplatin-intermediate group and cisplatin-resistant group. (**B**) Immunohistochemical staining of cisplatin-resistant markers in the derived organoids. Quantification of staining intensities for the indicated markers performed in 19 organoid samples. Scale bars, 20 μm. (**C**) Immunohistochemical staining of cisplatin-resistant markers in tumor specimens of the whole cohort. Quantification of staining intensities for the indicated markers performed in 45 BTC tissue samples. Scale bars, 50 μm. (**D**) Immunohistochemical staining of cisplatin-sensitive markers in the derived organoids. Quantification of staining intensities for the indicated markers performed in 19 organoid samples. Scale bars, 20 μm. (**E**) Immunohistochemical staining of cisplatin-sensitive markers in tumor specimens of the whole cohort. Quantification of staining intensities for the indicated markers performed in 45 BTC tissue samples. Scale bars, 50 μm. (**F**) Pathways enriched in cisplatin-sensitive group and cisplatin-resistant group. Permutation test. Benjamini-Hochberg (BH) adjusted p value < 0.05. NES: Normalized enrichment scores.

Fig. S8

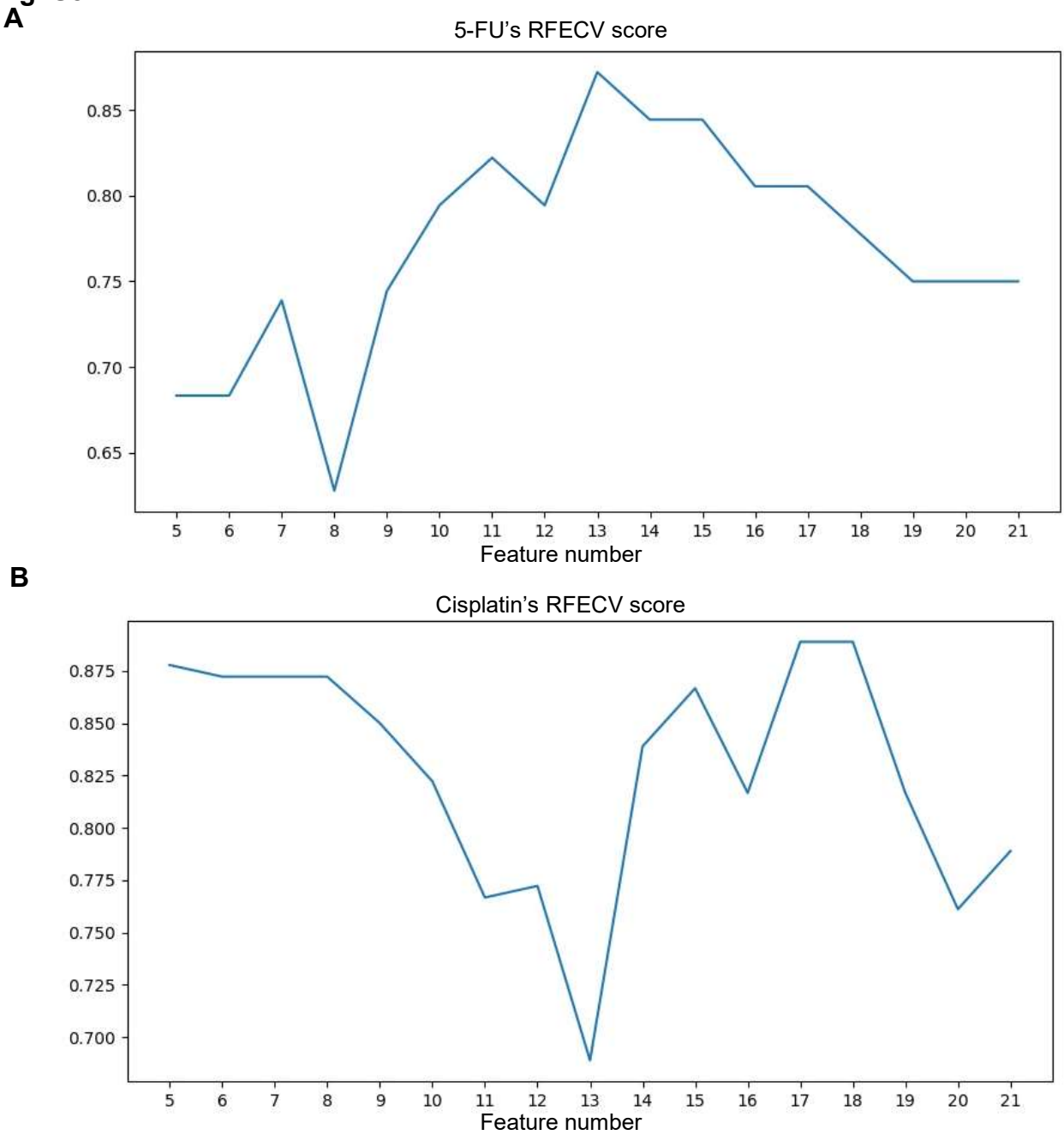


Figure S8. Transcriptional characteristics of cisplatin-sensitive group, related to Figure 7. (**A**) The RFECV score of 5-FU. (**B**) The RFECV score of cisplatin.

Table S2. Statistical analyses of clinicopathologic characteristics of patients, related to Figure 2.

Characteristics	Success (n=61)	Failure (n=21)	P-value
Age (years)	56 (32-84)	56 (37-78)	0.928
Gender, male	34 (55.7%)	9 (42.9%)	0.325
Bile duct stone	11/60 (18.3%)	5/21 (23.8%)	0.751
CA 19-9 (>37 U/ml)	36/60 (60.0%)	14/21 (66.7%)	0.795
CEA (>5 U/ml)	27/60 (45.0%)	7/21 (33.3%)	0.444
Tumor purity (%)	53 (28-89)	42 (21-56)	<0.001
Cancer stage by AJCC, 8th ed.			0.031
I-III	49(78.7%)	21(100%)	
IV	12(21.3%)	0(0%)	
Grading			0.172
I	0	1/18(5.6%)	
II	31/50(62.0%)	8/18(44.4%)	
III	19/50(38.0%)	9/18(50.0%)	
Pathological diagnosis			0.028
Extrahepatic cholangiocarcinoma	11 (18.0%)	4 (19.0%)	
Gallbladder carcinoma	4 (6.6%)	6 (28.6%)	
Intrahepatic cholangiocarcinoma	46 (75.4%)	11 (52.4%)	
Source			1.000
Surgery	58 (95.1%)	21 (100%)	
Ascites	2 (3.3%)	0	
Biopsy	1 (1.6%)	0	

AJCC, American Joint Committee on Cancer. Data are expressed as n (%) or median (range).

Table S3. AUC values of drug screening in patient-derived organoids, related to Figure 3.

Organoid ID	Gemcitabine (%)	Sensitivity of Gemcitabine	Cisplatin (%)	Sensitivity of Cisplatin	5-FU (%)	Sensitivity of 5-FU	SN-38 (%)	Sensitivity of SN-38	Oxaliplatin (%)	Sensitivity of Oxaliplatin	Mitomycin C (%)	Sensitivity of Mitomycin C	Paclitaxel (%)	Sensitivity of Paclitaxel
ECC-1T	2.99	Sensitive	34.38	Intermediate	28.03	Sensitive	2.95	Sensitive	40.30	Intermediate	7.61	Sensitive	1.62	Sensitive
ECC-2T	0.25	Sensitive	22.66	Sensitive	17.59	Sensitive	0.64	Sensitive	39.99	Intermediate	3.26	Sensitive	7.42	Sensitive
ECC-4T	5.10	Sensitive	37.20	Intermediate	30.73	Sensitive	1.17	Sensitive	49.63	Intermediate	4.68	Sensitive	1.68	Sensitive
ECC-8T	23.10	Sensitive	19.25	Sensitive	61.07	Sensitive	1.53	Sensitive	89.51	Resistant	15.86	Sensitive	83.43	Resistant
ECC-14T	0.58	Sensitive	2.30	Sensitive	7.25	Sensitive	0.30	Sensitive	27.58	Sensitive	4.32	Sensitive	3.58	Sensitive
ECC-15T	1.48	Sensitive	2.21	Sensitive	10.28	Sensitive	0.45	Sensitive	40.43	Intermediate	7.19	Sensitive	3.00	Sensitive
ECC-16T	2.75	Sensitive	17.63	Sensitive	21.85	Sensitive	0.59	Sensitive	61.34	Intermediate	12.45	Sensitive	16.06	Sensitive
ECC-19T	3.32	Sensitive	17.87	Sensitive	15.52	Sensitive	0.74	Sensitive	72.10	Resistant	22.90	Sensitive	81.02	Resistant
ECC-20T	1.27	Sensitive	8.41	Sensitive	20.60	Sensitive	1.23	Sensitive	31.92	Sensitive	6.99	Sensitive	32.72	Sensitive
ECC-21T	3.85	Sensitive	31.64	Sensitive	50.53	Intermediate	1.52	Sensitive	100.00	Resistant	12.27	Sensitive	63.13	Intermediate
ECC-26T	0.80	Sensitive	13.05	Sensitive	8.34	Sensitive	0.25	Sensitive	47.98	Intermediate	2.66	Sensitive	13.58	Sensitive
ECC-27T	1.07	Sensitive	12.04	Sensitive	13.20	Sensitive	0.29	Sensitive	26.21	Sensitive	3.36	Sensitive	10.83	Sensitive
GBC-4T	7.80	Sensitive	27.58	Sensitive	33.79	Intermediate	2.05	Sensitive	70.39	Resistant	9.05	Sensitive	2.57	Sensitive
GBC-9T	5.42	Sensitive	15.58	Sensitive	18.16	Sensitive	1.48	Sensitive	48.77	Intermediate	6.79	Sensitive	1.35	Sensitive
GBC-11T	8.42	Sensitive	66.51	Intermediate	45.17	Intermediate	2.43	Sensitive	90.98	Resistant	15.14	Sensitive	64.80	Intermediate
ICC-7T	3.26	Sensitive	29.11	Sensitive	26.63	Sensitive	0.55	Sensitive	35.16	Intermediate	6.87	Sensitive	17.98	Sensitive
ICC-8T	2.12	Sensitive	12.36	Sensitive	26.18	Sensitive	1.08	Sensitive	43.83	Intermediate	10.37	Sensitive	16.84	Sensitive
ICC-14T	19.44	Sensitive	30.83	Sensitive	31.52	Sensitive	7.86	Sensitive	63.97	Intermediate	30.77	Sensitive	46.67	Intermediate
ICC-17T	2.58	Sensitive	35.21	Intermediate	0.82	Sensitive	30.09	Sensitive	33.55	Intermediate	7.38	Sensitive	29.68	Sensitive
ICC-21T	7.95	Sensitive	52.40	Intermediate	31.72	Sensitive	1.21	Sensitive	51.70	Intermediate	11.07	Sensitive	3.20	Sensitive
ICC-23T	11.68	Sensitive	56.34	Intermediate	42.67	Intermediate	1.61	Sensitive	79.91	Resistant	19.40	Sensitive	1.92	Sensitive

ICC-28T	3.43	Sensitive	20.97	Sensitive	23.30	Sensitive	0.58	Sensitive	45.78	Intermediate	7.41	Sensitive	6.90	Sensitive
ICC-29T	4.99	Sensitive	34.14	Intermediate	28.67	Sensitive	0.81	Sensitive	70.61	Resistant	14.35	Sensitive	33.08	Intermediate
ICC-31T	1.64	Sensitive	9.62	Sensitive	22.72	Sensitive	1.33	Sensitive	48.08	Intermediate	7.87	Sensitive	11.80	Sensitive
ICC-36T	5.40	Sensitive	44.20	Intermediate	22.91	Sensitive	1.01	Sensitive	100.00	Resistant	8.18	Sensitive	15.50	Sensitive
ICC-37T1	4.55	Sensitive	17.21	Sensitive	10.31	Sensitive	1.18	Sensitive	32.29	Sensitive	10.43	Sensitive	12.63	Sensitive
ICC-37T2	5.54	Sensitive	19.10	Sensitive	22.89	Sensitive	1.08	Sensitive	45.93	Intermediate	12.46	Sensitive	15.57	Sensitive
ICC-37T3	20.79	Sensitive	37.22	Intermediate	67.97	Resistant	2.93	Sensitive	77.55	Resistant	25.80	Sensitive	85.83	Resistant
ICC-38T	1.60	Sensitive	2.91	Sensitive	22.91	Sensitive	25.05	Sensitive	35.36	Intermediate	8.40	Sensitive	16.86	Sensitive
ICC-45T	26.04	Sensitive	16.64	Sensitive	52.01	Intermediate	9.41	Sensitive	56.17	Intermediate	18.32	Sensitive	50.09	Intermediate
ICC-46T	4.75	Sensitive	28.88	Sensitive	22.73	Sensitive	0.37	Sensitive	34.40	Intermediate	6.37	Sensitive	10.72	Sensitive
ICC-46T-MA	2.52	Sensitive	8.39	Sensitive	6.05	Sensitive	0.25	Sensitive	39.17	Intermediate	4.31	Sensitive	5.84	Sensitive
ICC-47T	7.43	Sensitive	20.71	Sensitive	15.69	Sensitive	5.12	Sensitive	100.00	Resistant	8.76	Sensitive	20.95	Sensitive
ICC-49T	6.61	Sensitive	82.08	Resistant	53.12	Intermediate	2.28	Sensitive	100.00	Resistant	11.89	Sensitive	31.35	Sensitive
ICC-50T1	4.06	Sensitive	100.00	Resistant	41.77	Intermediate	1.60	Sensitive	100.00	Resistant	26.82	Sensitive	26.69	Sensitive
ICC-50T2	1.45	Sensitive	53.75	Intermediate	16.72	Sensitive	0.90	Sensitive	79.37	Resistant	7.21	Sensitive	8.95	Sensitive
ICC-53T	2.85	Sensitive	26.19	Sensitive	14.81	Sensitive	1.35	Sensitive	35.55	Intermediate	9.00	Sensitive	4.98	Sensitive
ICC-57T	3.08	Sensitive	40.42	Intermediate	31.27	Sensitive	1.25	Sensitive	88.22	Resistant	23.01	Sensitive	41.81	Intermediate
ICC-58T	5.61	Sensitive	49.31	Intermediate	14.81	Sensitive	3.77	Sensitive	55.87	Intermediate	7.50	Sensitive	30.29	Sensitive
ICC-62T1	28.82	Sensitive	12.86	Sensitive	30.45	Sensitive	17.41	Sensitive	60.01	Intermediate	11.65	Sensitive	34.34	Intermediate
ICC-63T	0.76	Sensitive	6.68	Sensitive	9.77	Sensitive	0.30	Sensitive	34.68	Intermediate	10.88	Sensitive	0.98	Sensitive
ICC-65T	3.17	Sensitive	35.04	Intermediate	4.57	Sensitive	0.32	Sensitive	41.76	Intermediate	4.64	Sensitive	13.64	Sensitive
ICC-67T	9.53	Sensitive	100.00	Resistant	68.36	Resistant	1.72	Sensitive	95.46	Resistant	7.12	Sensitive	54.64	Intermediate
ICC-69T	23.46	Sensitive	44.19	Intermediate	45.51	Intermediate	2.85	Sensitive	72.10	Resistant	22.90	Sensitive	75.24	Resistant
ICC-71T	2.98	Sensitive	18.78	Sensitive	10.86	Sensitive	0.63	Sensitive	40.52	Intermediate	5.82	Sensitive	9.08	Sensitive
ICC-72T	2.44	Sensitive	13.24	Sensitive	19.06	Sensitive	1.74	Sensitive	39.11	Intermediate	11.98	Sensitive	6.45	Sensitive

ICC-73T-MA	54.45	Intermediate	54.36	Intermediate	93.09	Resistant	11.05	Sensitive	67.53	Resistant	7.94	Sensitive	39.98	Intermediate
GBC-10T	10.02	Sensitive	48.23	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
GBC-16T	NA	NA	35.94	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-4T	10.86	Sensitive	22.57	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-5T	3.08	Sensitive	40.42	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-16T	NA	NA	31.27	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-19T	NA	NA	41.81	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-20T	6.93	Sensitive	28.22	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-22T	NA	NA	17.47	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-26T	NA	NA	23.86	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-33T1	4.09	Sensitive	35.52	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-33T2	3.52	Sensitive	40.03	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-33T3	8.76	Sensitive	38.44	Intermediate	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-34T	NA	NA	23.01	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
ICC-62T2	26.64	Sensitive	14.53	Sensitive	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Sensitive:0-33%; Intermediate: 33-67%; Resistant: >67%; NA: Not available

Table S4. Clinical response of patients, related to Figure 5.

Organoid ID	Patient ID	Date of operation, diganosis or recurrence	Tumor stage	Type of chemotherapy	Chemotherapy regimens	Clinical response	Clinical response to therapies	Organoid treatment			Sensitivity	Correlation
								Drug	IC50 (μM)	AUC (%)		
ECC1T	ECC1T-P	Operation (20200803)	IIIc	Adjuvant chemotherapy	FOLFORINOX (5FU+Oxaliplatin +Irinotecan) *12	No recurrence (20220405)	Sensitive	5FU	9.131	28.03	Sensitive	yes
								Oxaliplatin	30.79	40.3	Intermediate sensitive	
								SN38 (Irinotecan)	0.005	2.95	Sensitive	
ECC8T	ECC8T-P	Operation (20201203)	IIIb	Adjuvant chemotherapy	AG (Gemcitabine+Paclitaxel) *6	Lymphatic metastasis (20211201)	Resistant	Gemcitabine	3.47	23.1	Sensitive	yes
								Paclitaxel	0.9257	83.43	Resistant	
ICC49T	ICC49T-P	Operation (20210329)	IV	Adjuvant chemotherapy	GEMOX (Gemcitabine+Oxaliplatin) *2	Lymphatic and lung metastasis (20220114)	Resistant	Gemcitabine	0.312	6.61	Sensitive	yes
					GP (Gemcitabine+Cisplatin) *6			Oxaliplatin	625.2	100.00	Resistant	
					Capecitabine *4			Cisplatin	515.1	82.08	Resistant	
								5FU (Capecitabine)	89.95	53.12	Intermediate sensitive	
ECC21T	ECC21T-P	Operation (20210602)	IIIc	Adjuvant chemotherapy	Capecitabine *8	No recurrence (20230427)	Sensitive	5FU (Capecitabine)	74.83	50.53	Intermediate sensitive	yes

ICC65T	ICC65T-P	Operation (20210705)	Ia	Adjuvant chemotherapy	Capecitabine *8	No recurrence (20220915)	Sensitive	5FU (Capecitabine)	0.0208	4.57	Sensitive	yes
ECC27T	ECC27T-P	Operation (20210917)	IVa	Adjuvant chemotherapy	GS (Gemcitabine+S-1) *6	No recurrence (20220914)	Sensitive	Gemcitabine	0.005	1.07	Sensitive	yes
								5FU (S-1)	0.7384	13.2	Sensitive	
ICC63T	ICC63T-P	Operation (20210621)	IIIb	Adjuvant chemotherapy	Capecitabine *8	Recurrence and bone metastasis (20220118)	Resistant	5FU	0.0893	9.77	Sensitive	no
ECC17T	ECC17T-P	Recurrence and liver metastasis (20210524)	IV	Palliative chemotherapy	GP (Gemcitabine+Cisplatin) *6	Partial response (20211011)	Sensitive	Gemcitabine	0.148	2.58	Sensitive	yes
								Cisplatin	75.86	35.21	Intermediate sensitive	
ICC50T	ICC50T-P	Recurrence and metastasis (20210713)	IV	Palliative chemotherapy	GP (Gemcitabine+Cisplatin) *4	Progressive disease, recurrence and liver metastasis (20211124)	Resistant	Gemcitabine	0.084	4.06	Sensitive	yes
								Cisplatin	184.8	100.00	Resistant	
ECC20T	ECC20T-P	Recurrence and metastasis (20210830)	IV	Palliative chemotherapy	GEMOX (Gemcitabine+Oxaliplatin) *8	Partial response (20220826)	Sensitive	Gemcitabine	0.021	1.27	Sensitive	yes
								Oxaliplatin	48.32	31.92	Sensitive	
ICC71T	ICC71T-P	Recurrence and metastasis (20211101)	IV	Palliative chemotherapy	GP (Gemcitabine+Cisplatin) *6	Partial response (20220803)	Sensitive	Gemcitabine	0.0029	2.98	Sensitive	yes
								Cisplatin	20.3	18.78	Sensitive	
ICC69T			IV				Sensitive	Gemcitabine	5.679	23.46	Sensitive	yes

	ICC69T-P	Metastasis (20220217)		Palliative chemotherapy	GP (Gemcitabine+Cisplatin) *6	Stable disease (20220804)		Cisplatin	72.43	44.19	Intermediate sensitive	
ICC73T-MA	ICC73T-P	Diganosis (20210929)	IV	Palliative chemotherapy	GP (Gemcitabine+Cisplatin) *1	Death (20211201)	Resistant	Gemcitabine	77.75	54.44	Intermediate sensitive	yes
					AG (Gemcitabine+Paclitaxel) *1			Cisplatin	110.2	54.36	Intermediate sensitive	
								Paclitaxel	0.0003	39.98	Intermediate sensitive	

Table S5. Reagents, related to STAR Methods section.

Name	Vendor	catalog
Cisplatin	Selleck	S1166
Oxaliplatin	Selleck	S1224
Gemcitabine	Selleck	S1714
5-Fluorouracil	Selleck	S1209
SN-38	Selleck	S4908
Paclitaxel	Selleck	S1150
Mitomycin C	Selleck	S8146
B-27™ Supplement, serum free	Thermo Fisher Scientific	17504044
N-2 Supplement	Thermo Fisher Scientific	17502048
Nicotinamide	Sigma	N0636
GlutaMAX	Gibco	35050061
HEPES	Gibco	15630080
N-acetyl-L-cysteine	Sigma	A9165-5G
Gastrin-1, human	Genscript	PR12740
Recombinant Human EGF	Peprotech	AF-100-15
Human HGF	Novoprotein	CJ72-50
Recombinant Human FGF-10	Peprotech	100-26
A 83-01	TOCRIS	2939
Y-27632	Selleck	S1049
Recombinant Human Noggin	Peprotech	120-10C

Matrigel	Corning	356231
Advanced DMEM/F-12	Gibco	12634028
Forskolin	Sigma	F6886-10MG
Pen/Strep	Gibco	15140122
Collagenase type IV	Sigma	C5138
dispase type II	Invitrogen	17101015
DeadEnd™ Fluorometric TUNEL System	Promega	G3250
Anti-Cytokeratin 7	Abcam	ab68459
Anti-Cytokeratin 19	Abcam	ab76539
Anti-Ki67	Abcam	ab15580
Anti-PIGR	Abcam	Ab275020
Anti-NAT8L	Abcam	Ab76842
Anti-APOD	Abcam	Ab256496
Anti-THBS4	Abcam	Ab263898
Anti-IGFBP1	CST	31025S
Anti-CST1	Proteintech	16025-1-AP
Anti-TFF2	Abcam	ab267474
Anti-ABCB11	Proteintech	18990-1-AP
Anti-TP73	Abcam	ab189896
Anti-MCM2	Abcam	ab108935
Anti-CDT1	Proteintech	14382-1-AP

Anti-AIF1L	Abcam	ab204493
Anti-DNAJC12	Proteintech	12338-1-AP
Anti-HTR7	Proteintech	13830-1-AP
Anti-IFRD1	Santa cruz	sc-515012
Anti-DLL4	Proteintech	21584-1-AP
Anti-CEACAM5	Origene	TA803413
Anti-ZC3H12D	Proteintech	24991-1-AP
Anti-CLDN18	Proteintech	21126-1-AP
Anti-ARID3A	Proteintech	14068-1-AP
REAL™ EnVision™ Detection System	Dako	K500711-2
CellTiter-Glo assay	Promega	G7570
PureLink™ RNA	Thermo Fisher	12183020