

Table S1 IC₅₀ values for different drugs, co-culture groups, and patients

Drug	Groups	Patients ID and IC ₅₀ (μM)									
		LC-3	LC-8	LC13	LC-16	LC-18	LC-19	LC-21	LC-22	LC-23	LC-24
Cisplatin	2D-LC	23.88	17.4	11.049	16.11	12.62	13.11	5.113	6.97	2.03	3.049
	Mono-LC	26.41	27.5	26.41	25.9	36.97	9.69	21.98	11.99	1.57	2.726
	3D-2-LC_1	25.58	14.25	25.58	30.67	19.96	23.68	32.51	3.521	12.70	4.999
	3D-2-LC_2	13.06	10.03	13.06	10.61	6.493	21.25	17.54	14.6	24.15	23.41
	3D-3-LC	27.77	10.81	22.65	16.29	12.79	3.365	5.020	8.692	6.377	3.525
Carboplatin	2D-LC	62.02	53.11	46.87	129.9	43.8	69.9	188.9	196.8	33.26	46.35
	Mono-LC	99.8	95.52	91.2	72.8	196.5	64.5	211.6	92.87	6.483	11.4
	3D-2-LC_1	71.71	99.01	82.09	53.9	118.5	42.3	–	26.73	–	67.25
	3D-2-LC_2	78.43	74.56	104.1	89.4	59.91	79.88	–	137.5	–	215.4
	3D-3-LC	100.6	69.66	93.71	73.13	115.7	46.49	47.05	94.28	50.01	27.76
Paclitaxel	2D-LC	23.12	34.13	34.59	37.96	83.42	67.96	16.43	136.2	17.57	24.59
	Mono-LC	31.16	40.58	30.21	44.62	41.12	38.4	23.01	215.2	45.67	42.09
	3D-2-LC_1	29.47	41.5	80.17	40.67	98.28	81.7	48.21	–	–	47.67
	3D-2-LC_2	42.83	50.58	29.82	31.49	27.21	53.05	67.89	–	–	95.41
	3D-3-LC	22.3	69.15	27.38	30.76	173.5	26.5	204.5	31.72	154.3	66.62
Vinorelbine	2D-LC	9.545	9.62	7.72	13.33	15.07	33.33	3.788	5.742	4.171	5.72
	Mono-LC	18.01	16.7	28.73	–	12.68	42.1	14.1	28.3	0.2251	4.636
	3D-2-LC_1	18.65	18.49	26.36	–	9.075	112.3	–	40.49	–	41.72
	3D-2-LC_2	42.71	24.03	14.69	–	46.3	93.49	53.2	96.35	–	29.51
	3D-3-LC	33.01	11.93	8.212	–	38.16	4.056	31.92	65.22	38.36	11.42
Gemcitabine	2D-LC	37.83	27.48	48.44	36.47	14.1	36.47	41.54	23.62	8.752	6.156
	Mono-LC	52.15	57.29	40.72	–	–	–	22.77	2.737	1.972	46.74
	3D-2-LC_1	42.33	25.45	54.23	–	48.9	–	–	87.85	–	69.29
	3D-2-LC_2	45.37	43.78	67.82	–	40.8	146.7	47.02	61.33	–	56.4
	3D-3-LC	37.96	34.88	44.26	–	56.13	–	39.65	57.01	63.57	40.19
Gefitinib	2D-LC	7.619	4.748	7.6	6.01	11.93	0.9691	10.5	7.463	3.99	9.216
	Mono-LC	13.35	8.661	3.129	3.994	1.576	6.01	0.7533	20.39	0.245	22.46
	3D-2-LC_1	7.336	9.077	9.491	2.895	3.65	12	6.91	18.4	8.74	25.81
	3D-2-LC_2	13.32	11.22	2.781	2.312	0.907	19.74	8.95	12.4	11.25	20.9
	3D-3-LC	11.39	11.41	4.198	4.656	23.56	4.990	10.06	13.62	9.908	23.70
Osimertinib	2D-LC	2.51	4.282	1.003	4.11	2.619	0.762	3.535	7.113	2.337	2.003
	Mono-LC	4.063	6.91	4.731	5.301	1.192	1.073	3.113	4.272	0.413	1.786
	3D-2-LC_1	4.319	2.91	4.099	4.536	3.597	3.15	4.92	17.38	4.512	3.145
	3D-2-LC_2	6.149	3.693	1.834	1.955	6.426	4.69	3.98	14.14	6.798	4.607
	3D-3-LC	4.364	1.963	6.178	5.641	4.348	1.237	7.244	5.930	7.63	7.163
Almonertinib	2D-LC	1.904	2.289	1.755	2.665	3.246	4.665	5.743	0.6524	5.127	1.049
	Mono-LC	3.819	2.269	4.851	5.67	1.385	5.73	1.004	3.726	1.583	4.433
	3D-2-LC_1	4.28	2.652	2.842	3.71	1.23	8.334	0.937	5.19	6.92	5.661
	3D-2-LC_2	6.638	5.897	5.086	6.19	5.315	8.665	4.97	4.91	8.74	9.096
	3D-3-LC	5.397	4.942	5.794	6.94	4.611	7.813	5.743	15.72	5.127	11.18

2D-LC: 2D cultured lung cancer cells; Mono-LC: lung cancer cells cultured in 3D conditions; 3D-2-LC_1: CRLCs-CAFs co-culture; 3D-2-LC_2: CRLCs-HUVECs co-culture; 3D-3-LC: CRLCs-CAFs-HUVECs co-culture. IC₅₀, half maximal inhibitory concentration.

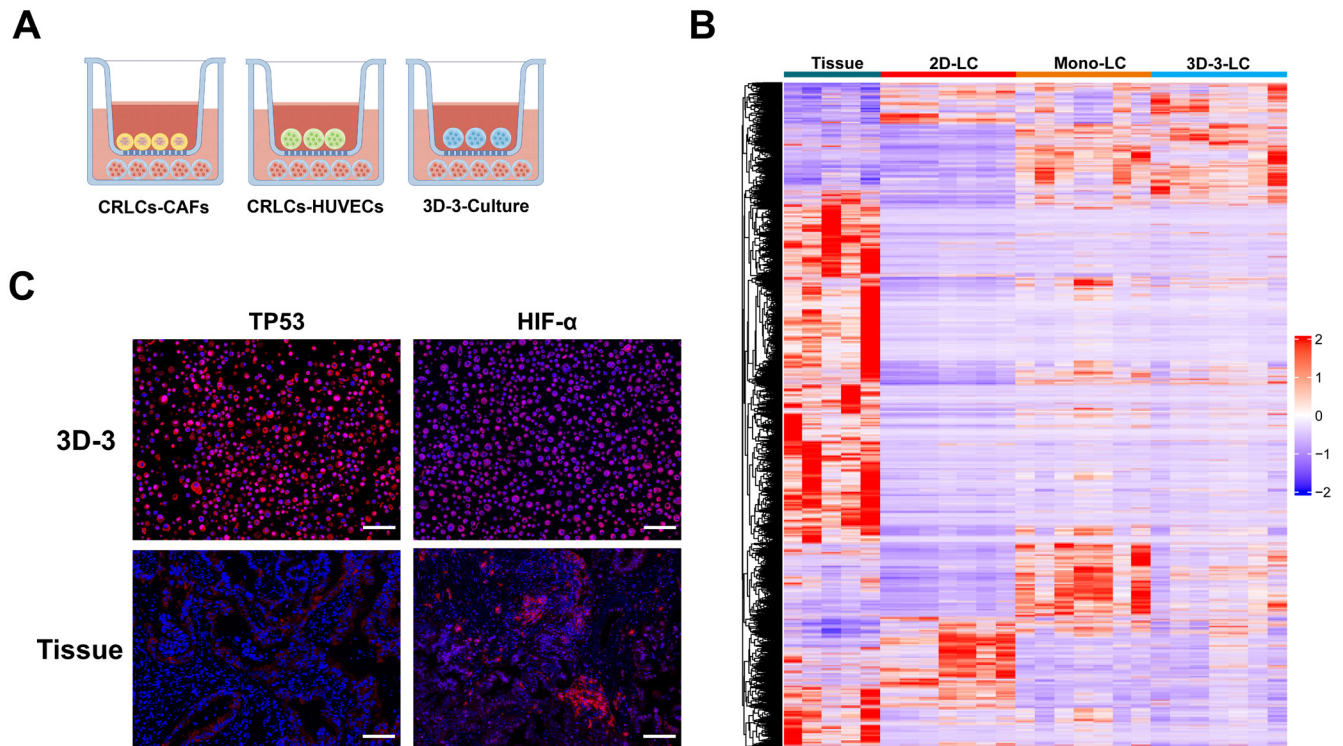


Figure S1 Transcriptome sequencing results of different 3D co-cultured microcapsules. (A) In the Western blotting and transcriptome sequencing analyses, CRLCs were co-cultured with CAFs and HUVECs through indirect co-culture. The upper layer contains the 3D microcapsules of CRLCs, while the lower layer includes the 3D microcapsules of stromal cells, Mono-CAFs, Mono-HUVECs, and CAFs-HUVECs. (B) The heatmap displays the fold-change differences in gene expression levels among the co-culture groups (tissue, 2D-LC, Mono-LC, 3D-3-LC). There is a certain degree of heterogeneity in gene expression of CRLCs among the different co-culture groups. (C) Immunofluorescence results of the 3D-3 hydrogel microcapsules alongside lung cancer tissue. Cells were stained with DAPI (blue) to indicate cell nuclei, and target proteins in CRLCs were marked with TP53 (red) and HIF- α (red). All scale bars represent 100 μ m. Tissue: lung cancer tissue; 2D-LC: 2D cultured lung cancer cells; Mono-LC: lung cancer cells cultured in 3D conditions; 3D-3-LC: CRLCs-CAFs-HUVECs co-culture. 2D, two-dimensional; 3D, three-dimensional; CAFs, cancer-associated fibroblasts; CRLCs, conditionally reprogrammed lung cancer cells; DAPI, 4',6-diamidino-2-phenylindole; HUVECs, human umbilical vein endothelial cells.