Table SI. Primer sequences used for reverse transcription-quantitative PCR.

Gene	Forward (5'-3')	Reverse (5'-3')
β-ACTIN	AAACTGGAACGGTGAAGGTG	AGAGAAGTGGGGTGGCTTTT
CHAC1	CCAGTGCTGCTGCTAACC	CTACTATCCCTCATCCAGCCT
ULBP1	GTCACAAAGTCAGAGATGGTGG	TAGTGGGATTGCGGGATTGA
PCK2	GCAGCAGAACACAAAGGGAA	GATCCAGTCTAGCACCCGAG
VLDLR	GCAGGGCAGATGTCACTACT	TCTTCAGACAGGTGTAGTGGAG
FDPS	AGGACAACAAATGCAGCTGG	GGTGCTGCGTACTGTTCAAT
HDAC2	TAGATGGGTGAGAGTGGTGC	ACAGAGGCATCAAGATCCCC
ACTA2	CTGTTCCAGCCATCCTTCAT	GCTGGAAGGTGGACAGAGAG

CHAC1, glutathione-specific γ-glutamylcyclotransferase 1; ULBP1, UL16 binding protein 1; PCK2, phosphoenolpyruvate carboxykinase 2; VLDLR, very low density lipoprotein receptor; FDPS, farnesyl diphosphate synthase; HDAC2, histone deacetylase 2.

Table SII. Upregulated genes associated with E7386 concentrations 24 h after the addition of E7386 to the colorectal cancer organoids compared with the control.

Name	Correlation	GB_ACC	GENE_SYMBOL	ENSEMBL_ID
A_33_P3376971	0.91	NM_024111	CHAC1	ENST00000617961
A_23_P41114	0.91	NM_005213	CSTA	ENST00000264474
A_33_P3376965	0.91	NM_024111	CHAC1	ENST00000444189
A_23_P259692	0.90	NM_058179	PSAT1	ENST00000376588
A_23_P17354	0.88	NM_024034	GDAP1L1	
A_24_P100761	0.86	NM_017679	BCAS3	ENST00000587294
A_33_P3237634	0.86	NM_004089	TSC22D3	ENST00000372383
A_33_P3422802	0.86	NM_025218	ULBP1	ENST00000229708
A_23_P104318	0.84	NM_019058	DDIT4	ENST00000307365
A_33_P3422810	0.82	NM_025218	ULBP1	ENST00000229708
A_23_P128817	0.81	NM_004563	PCK2	ENST00000559503
A_21_P0007913	0.81			ENST00000413591
A_33_P3413905	0.81	NM_024866	ADM2	ENST00000395738
A_33_P3416414	0.81			ENST00000518968
A_23_P421811	0.81	NM_152503	MROH8	ENST00000466091

A_23_P145694	0.80	NM_001673	ASNS	
A_23_P259621	0.80	NM_032464	LAT2	ENST00000460943
A_23_P37892	0.80	NM_133443	GPT2	ENST00000569193
A_23_P126103	0.80	NM_001902	CTH	ENST00000370938
A_19_P00315804	0.80	NR_015375	VLDLR-AS1	
A_33_P3363188	0.79	NR_033856	FLJ43315	
A_21_P0013514	0.79		XLOC_l2_014504	
A_23_P85783	0.79	NM_006623	PHGDH	ENST00000369407
A_23_P161634	0.79	NM_025128	MUS81	ENST00000524647
A_23_P300847	0.78	AF469204	MIR1247	ENST00000555882
A_33_P3353051	0.78	NM_001287483	C6orf48	
A_21_P0013512	0.77			ENST00000518311
A_33_P3297444	0.77	NM_032548	ABTB1	ENST00000464431
A_21_P0010773	0.77	NR_033856	FLJ43315	ENST00000623201
A_21_P0013475	0.76			ENST00000511103
A_33_P3268532	0.76	NM_001018073	PCK2	ENST00000396973
A_33_P3352432	0.76	NM_001129899	KRBOX4	
A_23_P157766	0.75	NM_00103939	SPATA6L	ENST0000040686

		5		1
A_23_P205913	0.75	NM_004727	SLC24A1	
A_24_P221485	0.75			ENST00000439132
A_23_P108342	0.75	NM_016536	ZNF571	ENST00000358744
A_23_P21134	0.75	NM_004083	DDIT3	ENST00000618206
A_22_P00023928	0.75	BX647685	lnc-RP11-293M10.1.1-1	
A_24_P235266	0.75	NM_001001555	GRB10	
A_19_P00800555	0.74		lnc-UQCRFS1-7	
A_24_P915196	0.74	NM_153045	C9orf91	ENST00000374049
A_33_P3281408	0.73	NM_001127401	YPEL5	
A_23_P43476	0.73	NM_003383	VLDLR	
A_23_P120316	0.72	NM_006636	MTHFD2	
A_33_P3240538	0.72	NM_016262	TUBE1	ENST00000368662
A_33_P3764802	0.72	NM_012241	SIRT5	ENST00000379250
A_33_P3831730	0.72		lnc-NDUFA4-2	
A_33_P3358295	0.72	NM_032548	ABTB1	ENST00000464431
A_24_P264664	0.72	NM_001271	CHD2	ENST00000394196
A_21_P0000629	0.72	NR_034072	SARS	
A_23_P117582	0.72	NM_130469	JDP2	
A_23_P166051	0.72	NM_031229	RBCK1	ENST00000356286

A_23_P401106	0.72	NM_002599	PDE2A	
A_23_P387184	0.71	NM_020464	NHSL1	ENST00000343505
A_33_P3276475	0.71	NM_020412	CHMP1B	ENST00000526991
A_33_P3236646	0.71	NM_198551	MIA3	
A_23_P101564	0.70	NM_019113	FGF21	ENST00000222157
A_33_P3389852	0.70	NM_017679	BCAS3	ENST00000590352
A_23_P415401	0.70	NM_001206	KLF9	ENST00000377126
A_23_P11984	0.70	NM_201649	SLC6A9	
A_22_P00000846	0.70	NR_024398	ZBED3-AS1	

Table SIII. Downregulated genes associated with E7386 concentrations 24 h after the addition of E7386 to the colorectal cancer organoids compared with that of the control.

NAME	Correlation	GB_ACC	GENE_SYMBOL	ENSEMBL_ID
A_33_P3253857	-0.87			ENST00000597330
A_33_P3240497	-0.80	AK095730		
A_33_P3522525	-0.79	NM_025196	GRPEL1	ENST00000504920
A_33_P3309924	-0.79	NM_001527	HDAC2	
A_21_P0013202	-0.78			ENST00000453012
A_33_P3214597	-0.77	NR_003500	RP9P	ENST00000381639
A_32_P179746	-0.75	XR_427741	LOC101929687	
A_22_P00004931	-0.75		lnc-DBX1-1	
A_24_P81947	-0.75	NM_014325	CORO1C	ENST00000420959
A_24_P114183	-0.74	NM_002004	FDPS	
A_23_P254573	-0.73	NM_014377	DNAJC2	ENST00000464253
A_24_P181585	-0.73	NM_018509	LRRC59	ENST00000225972
A_33_P3220095	-0.73	NM_001282933	ZNF341	
A_23_P153086	-0.73	NM_024805	RBFA	ENST00000593019
A_24_P160440	-0.73	NM_181462	MRPL55	
A_23_P111487	-0.73	NM_001128853	SRRT	
A_23_P403955	-0.73	NM_007375	TARDBP	ENST00000611008
A_22_P0001428	-0.72		lnc-SEPT11-1	

0				
A_32_P45738	-0.72	NM_002629	PGAM1	ENST00000334828
A_23_P157072	-0.72	NM_001037283	EIF3B	ENST00000475415
A_33_P3296099	-0.72			
A_23_P11859	-0.71	NM_016371	HSD17B7	ENST00000494450
A_24_P925314	-0.71	NM_000405	GM2A	ENST00000357164
A_22_P00014911	-0.71	AI384051	lnc-SLCO2B1-3	
A_33_P3316835	-0.70	AK002193	ZGRF1	ENST00000264370

Table SIV. Upregulated genes associated with E7386 concentrations 24 h after the addition of E7386 to the cancer-associated fibroblasts.

Name	Correlation	GB_ACC	GENE_SYMBOL	ENSEMBL_ID
A_21_P0013475	0.97			ENST00000511103
A_21_P0013512	0.97			ENST00000518311
A_23_P145694	0.97	NM_001673	ASNS	
A_21_P0009752	0.96		lnc-UQCRFS1-9	
A_21_P0013514	0.96		XLOC_l2_014504	
A_23_P128817	0.96	NM_004563	PCK2	ENST00000559503
A_24_P253251	0.96	NM_003045	SLC7A1	ENST00000380752
A_23_P259692	0.96	NM_058179	PSAT1	ENST00000376588
A_33_P3413905	0.96	NM_024866	ADM2	ENST00000395738
A_23_P85783	0.95	NM_006623	PHGDH	ENST00000369407
A_24_P154948	0.95	NM_002047	GARS	ENST00000470392
A_24_P335620	0.95	NM_003486	SLC7A5	ENST00000261622
A_33_P3416414	0.95			ENST00000518968
A_23_P120316	0.94	NM_006636	MTHFD2	
A_21_P0009753	0.94		LINC00662	ENST00000590677
A_23_P258964	0.94	NM_013417	IARS	ENST00000443024

A_23_P22224	0.94	NM_004095	EIF4EBP1	ENST00000338825
A_19_P00315627	0.93	XR_428440	LOC101930053	
A_23_P121875	0.93	NM_022483	C5orf28	ENST00000512085
A_23_P65262	0.93	NM_001278432	N4BP2L2	ENST00000509076
A_24_P270728	0.93	NM_001042483	NUPR1	
A_23_P165989	0.93	NM_080749	NEURL2	ENST00000372518
A_23_P70168	0.93	NM_152295	TARS	
A_33_P3209351	0.93	NM_013417	IARS	ENST00000375627
A_23_P120933	0.93	NM_001675	ATF4	ENST00000337304
A_33_P3535649	0.93	NM_032296	FLYWCH1	ENST00000416288
A_33_P3402615	0.93	NM_201649	SLC6A9	
A_21_P0000646	0.93	NR_034148	LINC00900	
A_33_P3268532	0.93	NM_001018073	PCK2	ENST00000396973
A_21_P0000629	0.92	NR_034072	SARS	
A_33_P3240538	0.92	NM_016262	TUBE1	ENST00000368662
A_23_P64661	0.92	NM_032496	ARHGAP9	ENST00000430041
A_23_P43317	0.92	NM_021619	PRDM12	ENST00000253008
A_23_P9614	0.92	NM_020142	NDUFA4L2	ENST00000555173
A_23_P149259	0.92	NM_032323	TMEM79	ENST00000495888

				1
A_33_P3353030	0.92	NM_003353	UCN	ENST00000296099
A_23_P15876	0.91	NM_052947	ALPK2	ENST00000361673
A_24_P221485	0.91			ENST00000439132
A_23_P166306	0.91	NM_000071	CBS	ENST00000617706
A_21_P0014094	0.91	AK096649		
A_23_P340722	0.91	NM_007235	XPOT	ENST00000449426
A_33_P3342430	0.91			ENST00000443279
A_23_P161399	0.91	NM_130439	MXI1	ENST00000485566
A_23_P150903	0.91	NM_018099	FAR2	ENST00000182377
A_24_P50753	0.91	NM_199040	NUDT4	
A_22_P00008272	0.91	NR_110453	CRNDE	
A_21_P0009754	0.91		lnc-UQCRFS1-9	
A_24_P364057	0.91	NM_032930	C11orf70	ENST00000530659
A_23_P353125	0.91	NM_152597	FSIP1	ENST00000350221
A_33_P3353051	0.91	NM_001287483	C6orf48	
A_23_P257578	0.91	NM_001035235	SRA1	
A_33_P3322288	0.91	NM_001134433	AZI2	ENST00000414162
A_23_P418485	0.91	NM_152587	C11orf65	ENST00000393088

				4
A_33_P3385957	0.91	NM_012263	TTLL1	ENST0000044076 1
A_22_P0001337 6	0.91	XM_00672259 4	lnc-RP11- 17M16.1.1-1	
A_24_P134834	0.90	NM_032276	RHBDD1	ENST0000039206 2
A_33_P3363188	0.90	NR_033856	FLJ43315	
A_23_P35082	0.90	NM_031459	SESN2	ENST0000025306 3
A_23_P422766	0.90	NM_172193	KLHDC1	ENST0000035933 2
A_33_P3764802	0.90	NM_012241	SIRT5	ENST0000037925 0
A_22_P0000827 1	0.90	NR_110454	CRNDE	
A_24_P95439	0.90	NM_00101443 7	CARS	
A_24_P115700	0.90	NM_078470	COX15	ENST0000037048 3
A_23_P115223	0.90	NM_006118	HAX1	ENST0000045791 8
A_32_P54503	0.90	NR_024451	JHDM1D-AS1	
A_19_P0032253 3	0.90	NR_110453	CRNDE	ENST0000056091 2

Table SV. Downregulated genes associated with E7386 concentration 24 h after the addition of E7386 to the cancer-associated fibroblasts.

Name	Correlation	GB_ACC	GENE_SYMBOL	ENSEMBL_ID
A_24_P101101	-0.94			ENST00000437414
A_23_P64860	-0.94	NM_003006	SELPLG	ENST00000550948
A_24_P276888	-0.94	NM_001199803	CENPO	ENST00000260662
A_32_P150735	-0.93			
A_32_P106732	-0.93	NM_020937	FANCM	ENST00000267430
A_23_P212639	-0.93	NM_004593	TRA2B	ENST00000456380
A_24_P203407	-0.93	NM_001080472	FITM2	
A_24_P323104	-0.93	NM_005219	DIAPH1	ENST00000253811
A_23_P51085	-0.93	NM_020675	SPC25	ENST00000611144
A_23_P102109	-0.93	NM_006000	TUBA4A	ENST00000486997
A_23_P81650	-0.92	NM_020199	C5orf15	ENST00000231512
A_32_P119197	-0.92	NM_001043352	TPM3	
A_33_P3392177	-0.92	NM_001256023	CLIC5	ENST00000484572
A_23_P30884	-0.92	NM_001288	CLIC1	ENST00000614673
A_24_P942604	-0.92	NM_006306	SMC1A	ENST00000375340
A_33_P3327165	-0.92	NM_206886	CCDC18	ENST00000447456
A_23_P308581	-0.91	NM_033112	RRP36	ENST00000244496
A_23_P45294	-0.91	NM_207318	FAM199X	ENST00000299906
A_23_P88731	-0.91	NM_002875	RAD51	
A_33_P3405500	-0.90	NM_014363	SACS	ENST00000382292
A_24_P349965	-0.90	NM_007109	TCF19	ENST00000400401
A_23_P434900	-0.90	NM_144570	HN1L	ENST00000248098
A_24_P181585	-0.90	NM_018509	LRRC59	ENST00000225972

Table SVI. Summary of the immunohistochemistry staining data for phosphoenolpyruvate carboxykinase 2, very low density lipoprotein receptor, β-catenin and α-smooth muscle actin expression in patient-derived xenografts from cases 21, 28 and 32 after treatment with E7380 twice a day for 14 days.

A, PCK2 (cytoplasmic granular positivity in carcinoma cells)									
Case #21				Case #28			Case #32		
Grade	+	++	+++	+	++	+++	+	++	+++
E7386 0 mg/kg	2	3	0	5	0	0	1	2	0
E7386 50 mg/kg	0	2	3	5	0	0	2	1	0
B, VLDLR (membranous positivity on apical surface in carcinoma cells)									
Case #21				Case #28			Case #32 (P=0.014)		
Grade	+	++	+++	+	++	+++	+	++	+++
E7386 0 mg/kg	5	0	0	5	0	0	0	3	0
E7386 50 mg/kg	3	2	0	5	0	0	0	0	3
C, β-catenin (nuclear positivity in carcinoma cells)									
Case #21				Case #28 (P=0.058)			Case #32		
Grade	+	++	+++	+	++	+++	+	++	+++
E7386 0 mg/kg	0	3	2	0	1	4	0	2	1
E7386 50 mg/kg	0	1	4	0	4	1	0	0	3
D, αSMA (cytoplasmic positivity in fibroblasts surrounding carcinoma cells)									
Case #21				Case #28 (P=0.058)			Case #32		
Grade	+	++	+++	+	++	+++	+	++	+++
E7386 0 mg/kg	0	3	2	1	4	0	1	2	0
E7386 50 mg/kg	2	2	1	4	1	0	0	3	0

+, <25%; ++, 25-75%; +++, 75%< positivity in sites of localization.