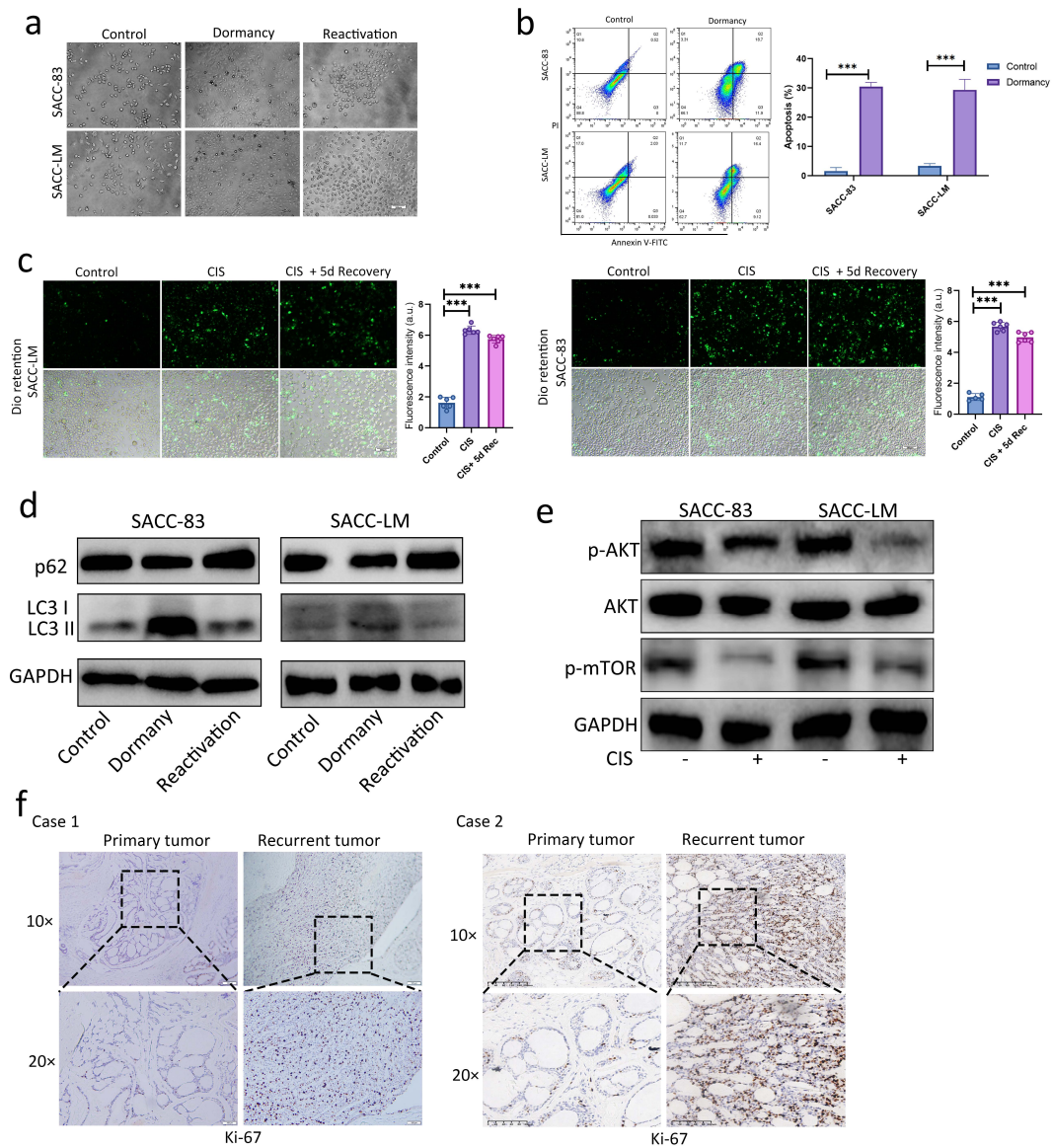
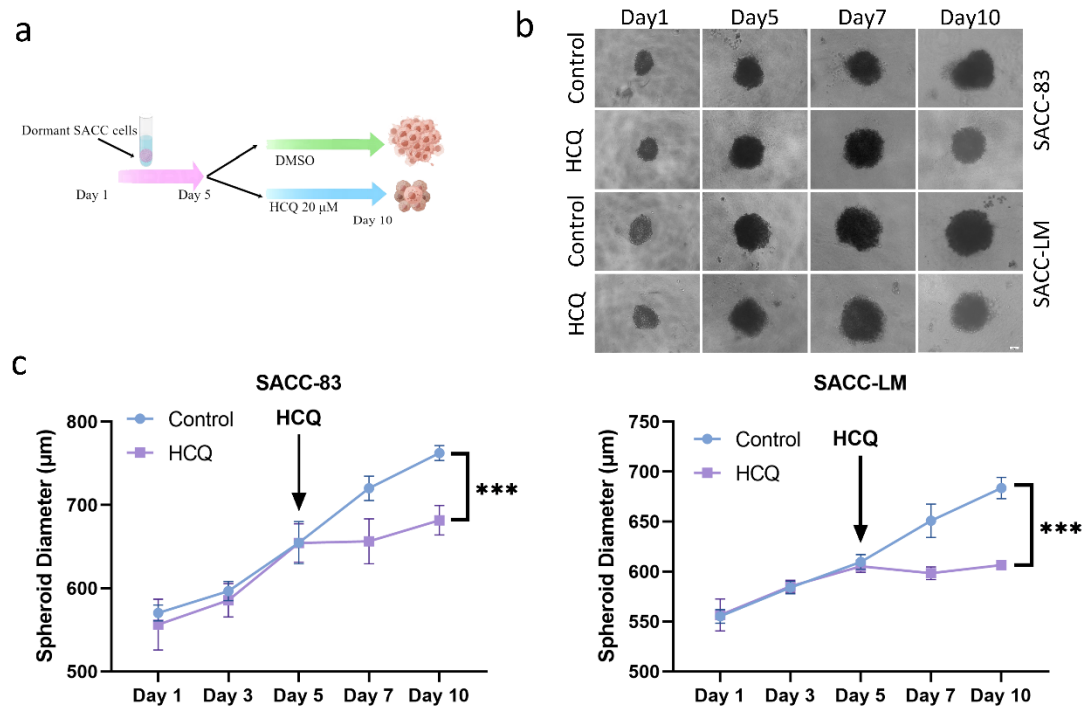


Supplementary Information

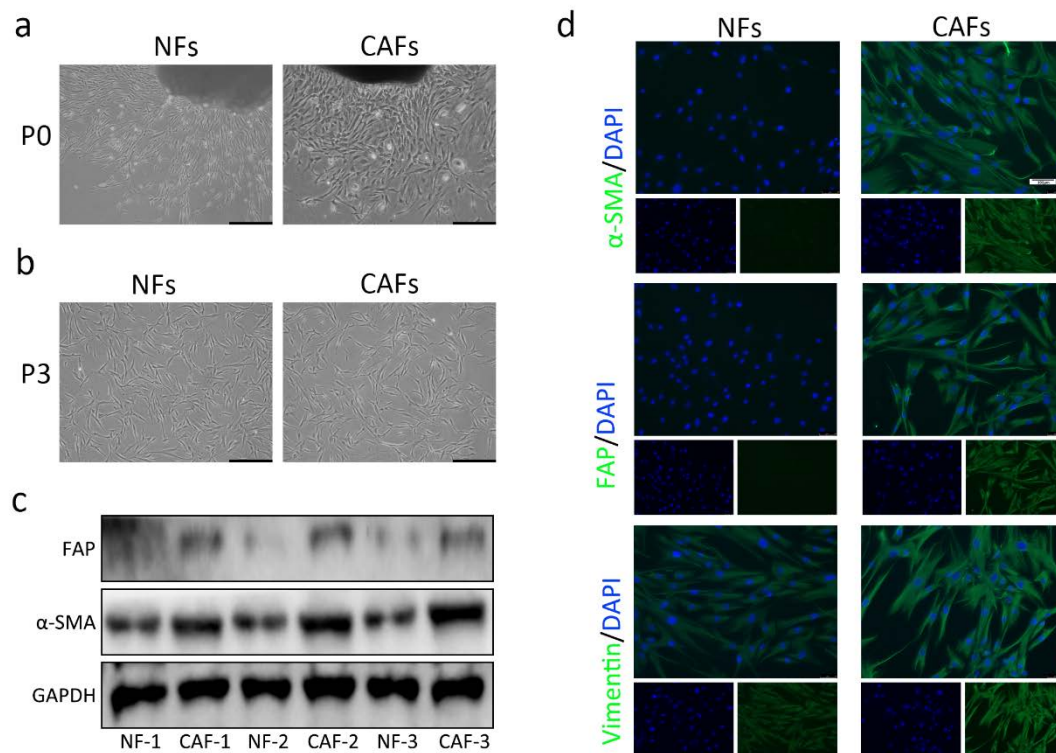
Supplementary Figures



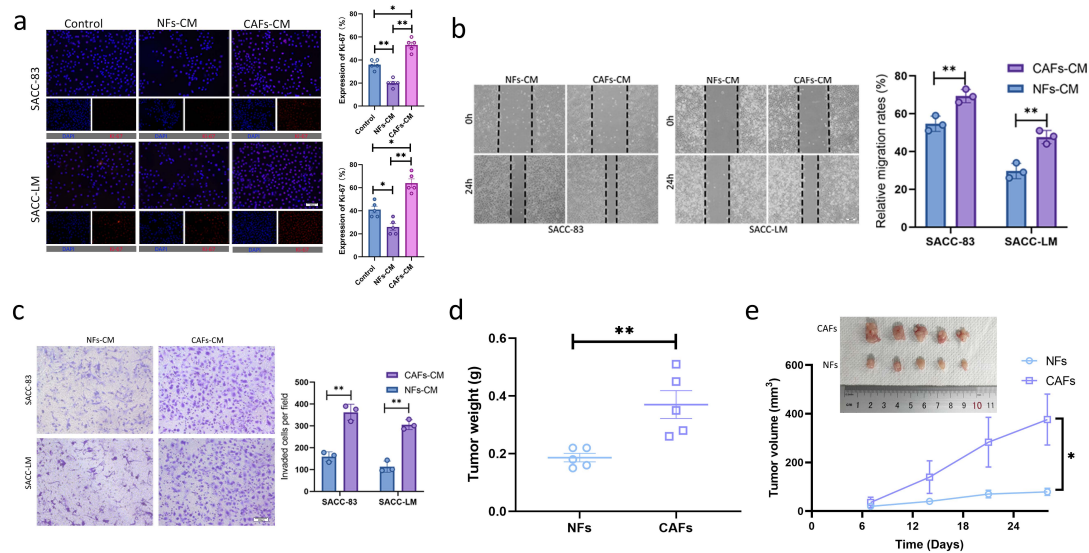
Supplementary Fig. 1: Dormant SACC tumor cells were autophagic. **a** The microscope images of dormant and reactivated SACC cells. **b** Flow cytometry analysis of apoptosis in SACC cells treated with cisplatin. **c** Dio staining analysis of SACC cells treated with cisplatin at different time points. **d** Western blot analysis of proteins obtained from dormant and reactivated SACC cells. **e** Western blot analysis of p-AKT, AKT, p-mTOR levels of SACC cells treated with cisplatin. **f** Assessment of Ki-67 in 6 SACC patients with recurrence after surgery and chemotherapy. Representative images of IHC.



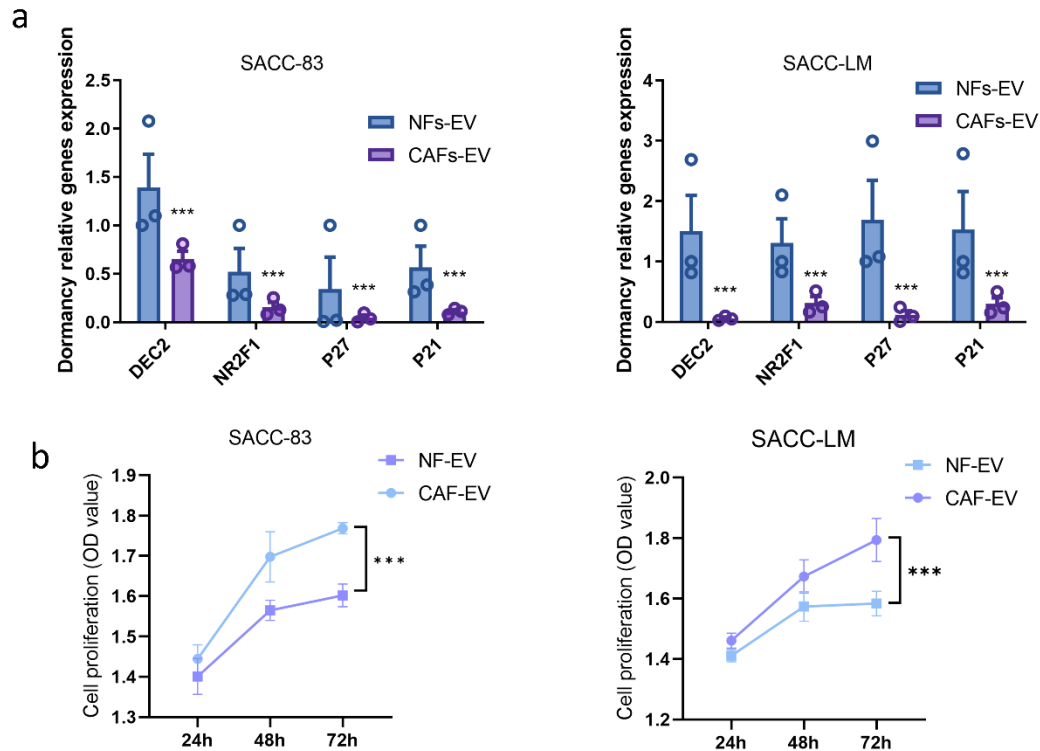
Supplementary Fig. 2: Autophagy inhibition reduced the sphere forming ability of dormant SACC cells. **a** Scheme of sphere formation assay in dormant SACC cells treated with HCQ. **b, c** Sphere formation assay on dormant SACC cells treated with HCQ (b). Scale bar, 200 μm . Statistical analysis of Sphere diameter (c).



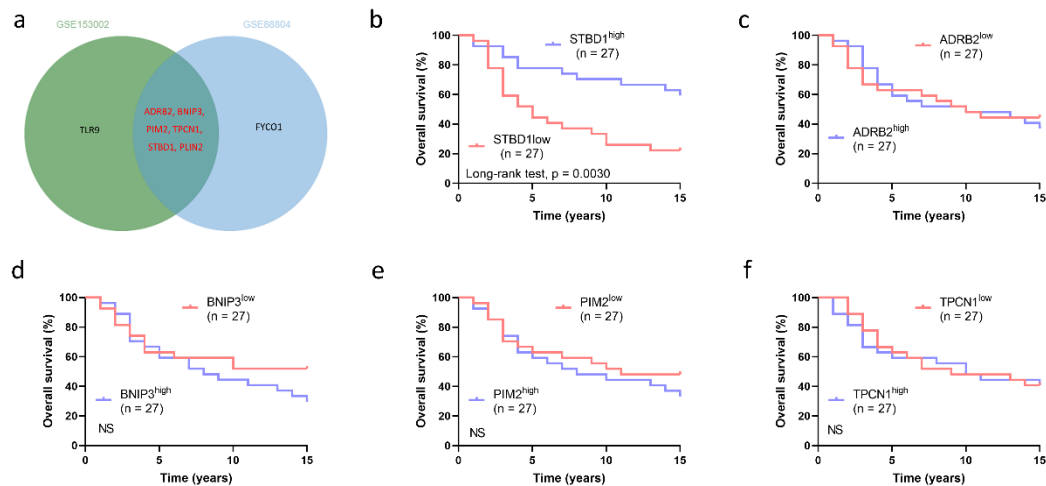
Supplementary Fig. 3: Identification of NFs and CAFs. **a, b** Representative cell morphology images of fibroblasts isolated from NSG and SACC tissues. Scale bar, 200 μm . **c** Western blot of α -SMA, vimentin, and FAP levels in fibroblasts. **d** Immunofluorescence analysis of α -SMA, vimentin, and FAP levels in fibroblasts. Scale bar, 100 μm .



Supplementary Fig. 4: CAFs promoted the proliferation, migration, invasion and tumorigenic ability of dormant SACC cells. **a** Assessment of Ki67 in dormant SACC cells treated with NFs-CM or CAFs-CM. Scale bar, 100 μm . **b, c** Migration and Transwell invasion assays in dormant SACC cells treated with NFs-CM or CAFs-CM. **d, e** The weights and volumes of the tumor were observed and measured.

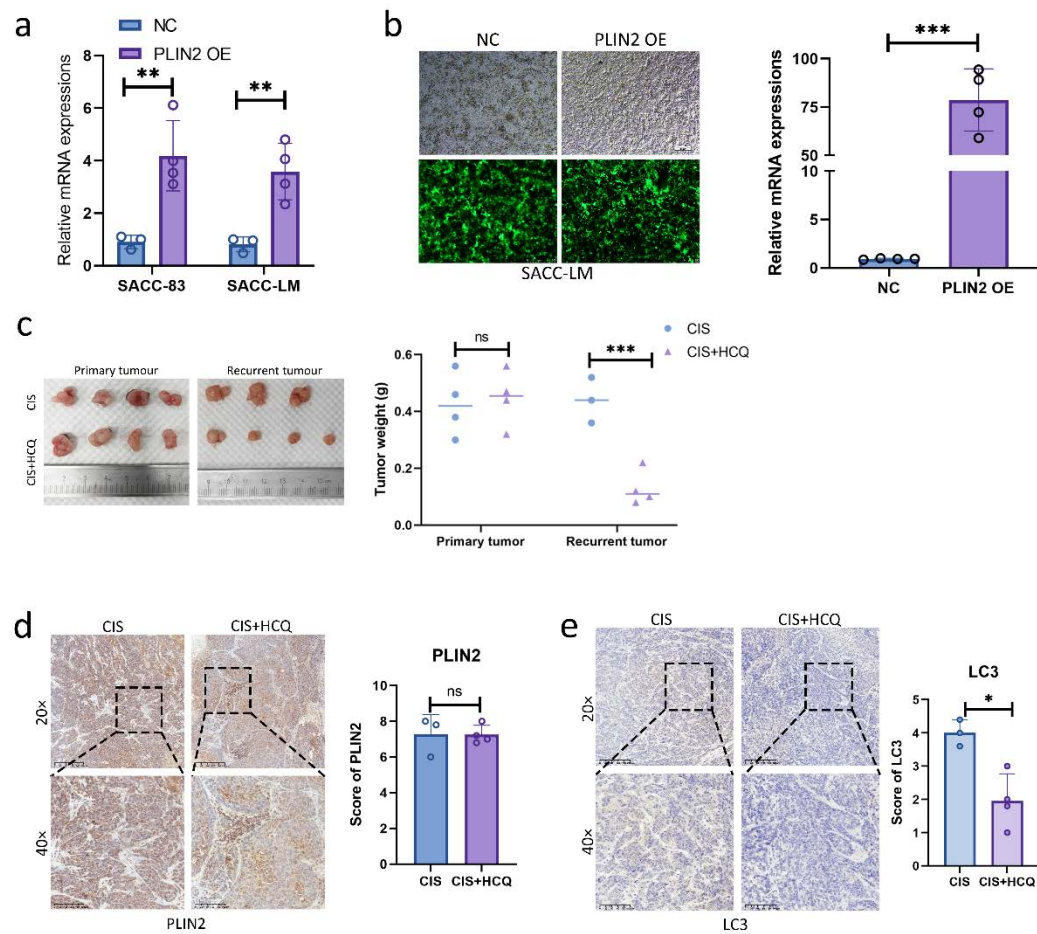


Supplementary Fig. 5: CAFs-EV contributed to the reactivation of dormancy SACC cells. **a** The proliferation assay of dormant SACC cells treated with NFs-EV or CAFs-EV. **b** qRT-PCR measured the relative mRNA level of dormancy in dormant SACC cells treated with NFs-EV or CAFs-EV.

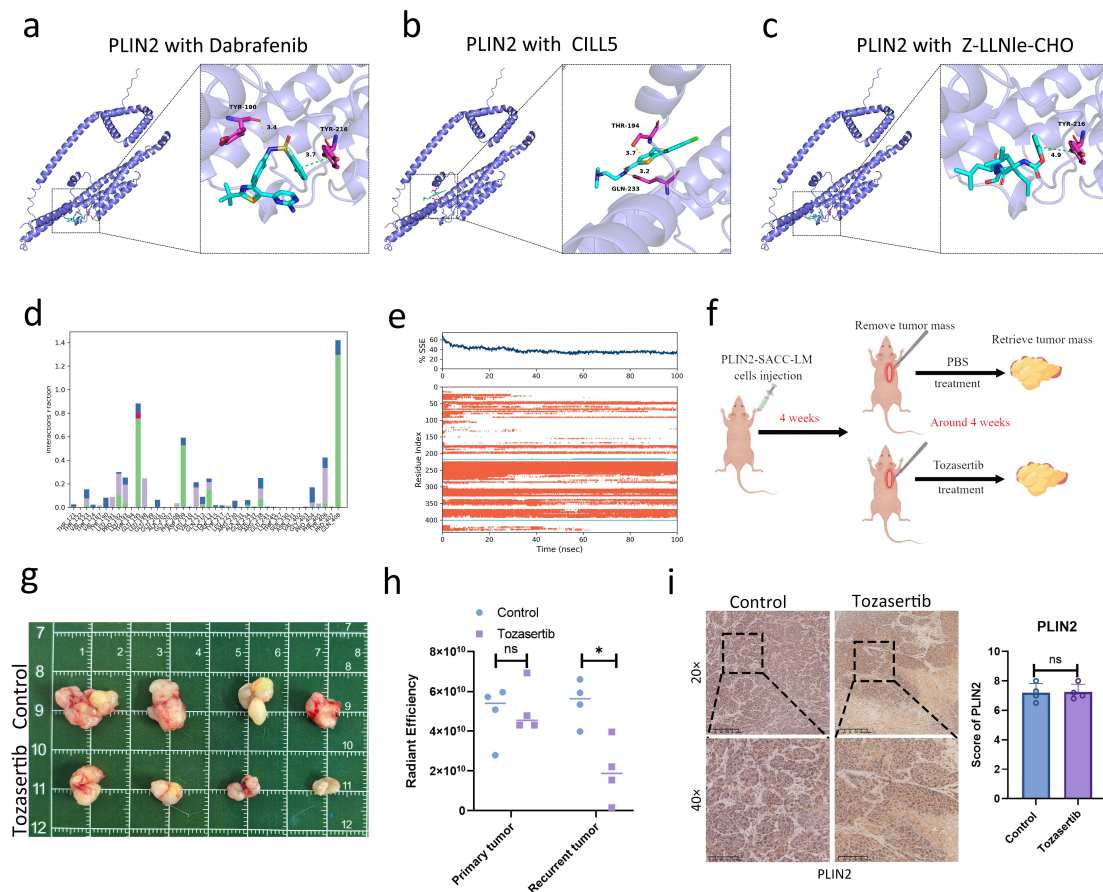


Supplementary Fig. 6: Correlation between candidate genes and prognosis in patients with SACC. **a** Venn diagram of candidate genes in GSE153002 and GSE88804 dataset. **b-f** Kaplan–Meier plots verified the correlation between STBD1,

ADRB2, BNIP3, PIM2 and TPCN1 expression and the overall survival rates in 54 SACC patients.



Supplementary Fig. 7: PLIN2-mediated autophagy induced tumor recurrence. a Overexpression efficiency test of PLIN2 in dormant SACC-83 and SACC-LM cells. **b** GFP-PLIN2-SACC-LM cells were constructed. **c** Macrograph of primary and recurrent tumors (left), tumor weights were calculated. **d, e** IHC analysis for PLIN2 and LC3 in recurrent tumor tissues.



Supplementary Fig. 8: Tozasertib markedly induced tumor recurrence. **a-c** The interactions analysis of PLIN2 and dabrafenib, CIL55 or Z-LLNle-CHO. **d, e** Analysis of the Tozasertib including interactions (d), secondary structural element (e). **f** Schematic diagram of tumor recurrence experiment in mice. **g-h** Macrograph of recurrent tumors (g), the radiant efficiencies of recurrent tumor were calculated (h). **i** IHC analysis for PLIN2 in recurrent tumor tissues.

Supplementary Tables

Supplementary Table 1

Primer Sequence Information	
qPCR: Human GAPDH Forward:	ACAAC TTTGGTATCGTGGAAGG
qPCR: Human GAPDH Reverse:	GCCATCACGCCACAGTTTC
qPCR: Human DEC2 Forward:	CTGATGCTGTTGCTCGGTTA
qPCR: Human DEC2 Reverse:	TGCAGACTCTGGGACATCTG
qPCR: Human NR2F1 Forward:	GCCTCAAAGCCATCGTGCTG
qPCR: Human NR2F1 Reverse:	CCTCACGTACTCCTCCAGTG
qPCR: Human P21 Forward:	TAGCAGCGGAACAAGGAG
qPCR: Human P21 Reverse:	AAACGGGAACCAGGACAC
qPCR: Human P27 Forward:	GGTTAGCGGAGCAATGCGCA
qPCR: Human P27 Reverse:	AACCGGCATTTGGGGAACCGTC
qPCR: Human Naong Forward:	AGATGCCTCACACGGAGACT
qPCR: Human Naong Reverse:	TCTGGAACCAGGTCTTCACC
qPCR: Human SOX2 Forward:	CACAAC TCGGAGATCAGCAA
qPCR: Human SOX2 Reverse:	GTT CATGTGCGCGTAACTGT
qPCR: Human Oct4 Forward:	CGAAAGAGAAAGCGAACCAG
qPCR: Human Oct4 Reverse:	TGAAGTGAGGGCTCCCATAG
qPCR: Human PLIN2 Forward:	TCCACTGTCCACCTGATTGA
qPCR: Human PLIN2 Reverse:	TGGCATGTAGTCTGGAGCTG

Supplementary Table 2. Clinical parameters of the SACC patients and their association with PLIN2 levels

Clinical index	patients (n=48)	PLIN2		P value
		High expression (≥ 5)	Low expression (< 5)	
Age				0.8544
	<60	30	6	
	≥ 60	18	4	
Gender				0.8822
	male	25	5	
	female	23	5	
Grade				0.0102*
	I-II	31	3	
	III	17	7	
Recurrence				
	yes	10	6	0.0006*
	no	38	4	