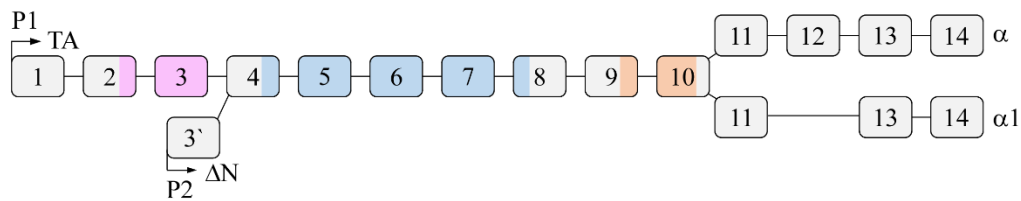
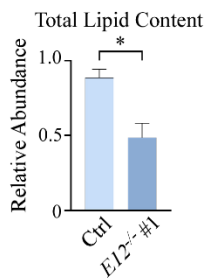
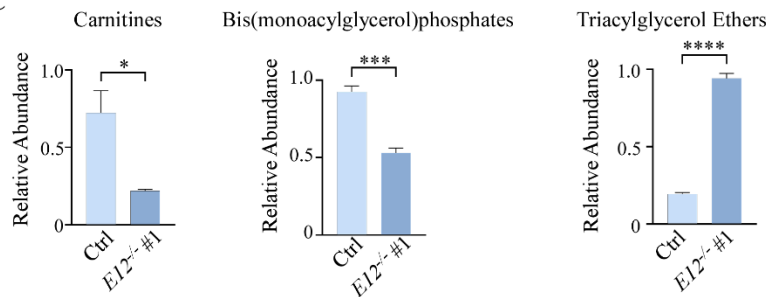
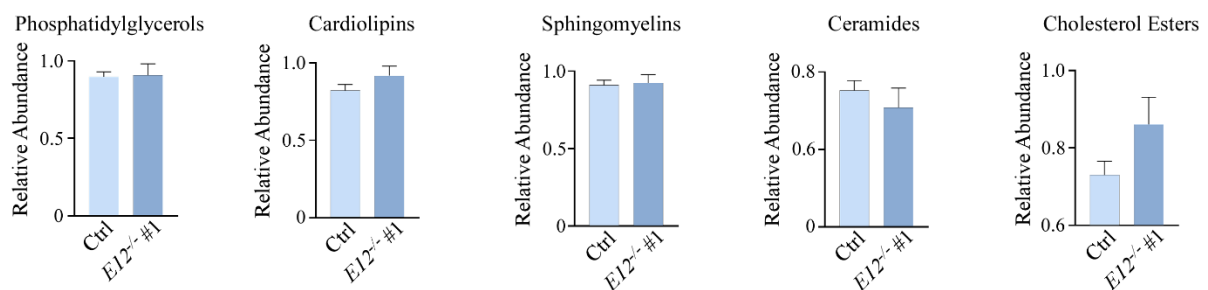


**A****B****C****D**

**Figure S1. Loss of *E12* alters the lipidome in H1299 cells.**

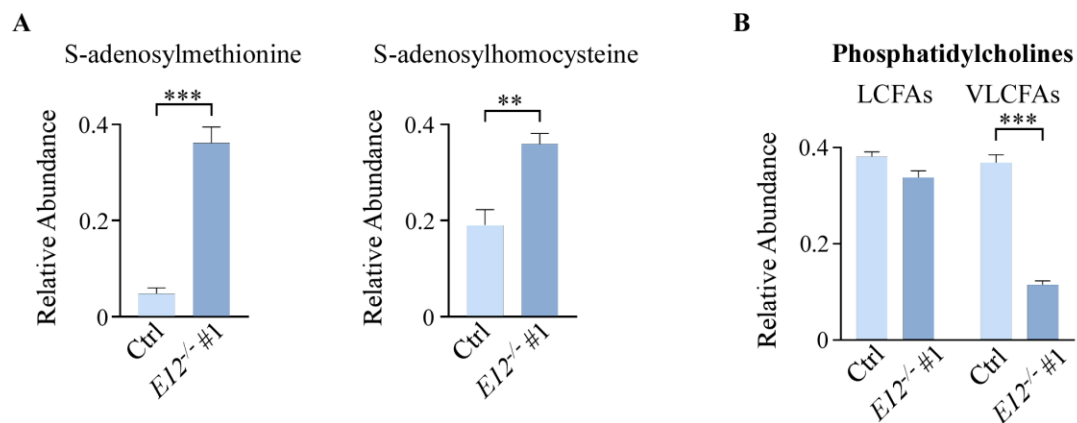
A. *TP73* diagram showing that loss of exon 12 leads to isoform switch from p73 $\alpha$  to p73 $\alpha$ 1. Pink region indicates transactivation domain, blue region indicates DNA binding domain, and orange region indicates oligomerization domain. P1: promoter 1; P2: promoter 2.

B. Relative abundance of total lipid content in isogenic control and *E12*<sup>-/-</sup> H1299 cells. Statistical significance was determined using Student's t-test.

C. Relative abundance of carnitines, bis(monoacylglycerol)phosphates, and triacylglycerol ethers in isogenic control and *E12*<sup>-/-</sup> H1299 cells. Statistical significance was determined using Student's t-test.

D. Relative abundance of phosphatidylglycerols, cardiolipins, sphingomyelins, ceramides, and cholesterol esters in isogenic control and *E12*<sup>-/-</sup> H1299 cells. Statistical significance was determined using Student's t-test.

For B-D. Data are presented as mean  $\pm$  SEM. n = 3 independent experiments. \* p < 0.05, \*\*\* p < 0.001, \*\*\*\* p < 0.0001.

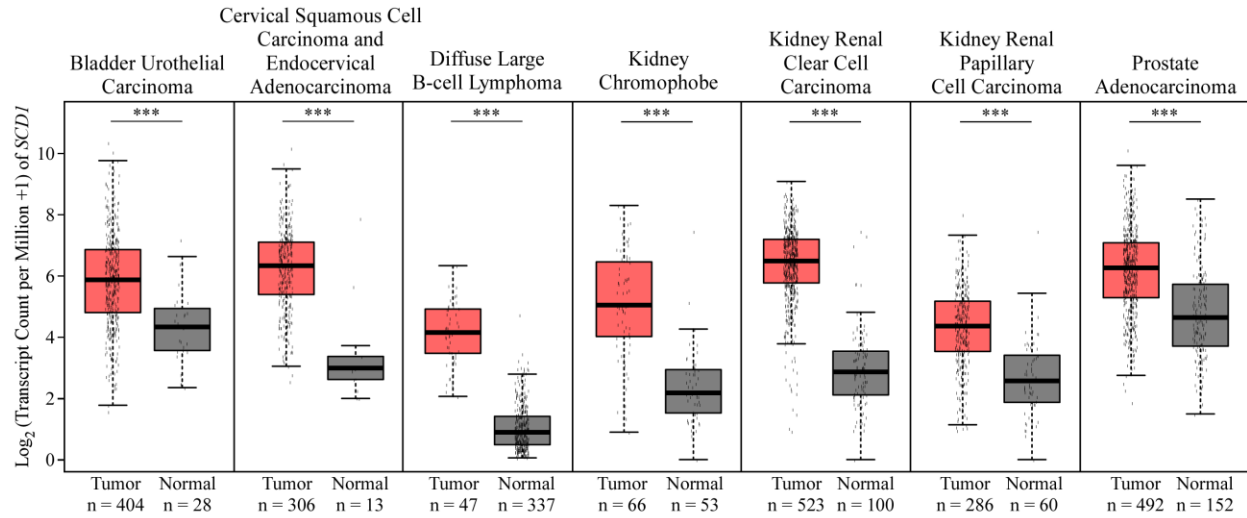
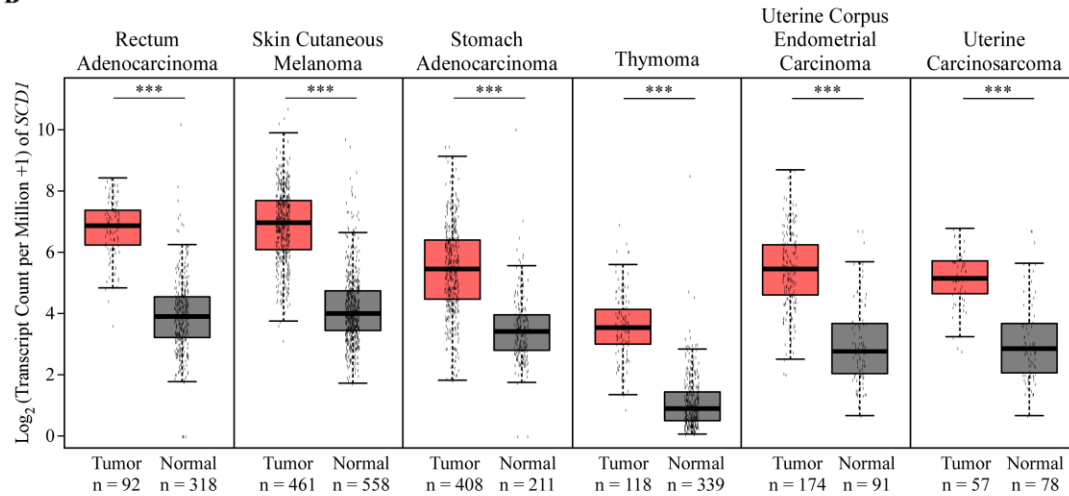


**Figure S2. Metabolites involved in PC synthesis are altered upon loss of *E12*.**

A. Relative abundance of S-adenosylmethionine and S-adenosylhomocysteine in isogenic control and *E12*<sup>-/-</sup> H1299 cell lines. Statistical significance was determined using Student's t-test.

B. Relative abundance of PCs containing (left) long-chain fatty acids (LCFAs) and (right) very long-chain fatty acids (VLCFAs) in isogenic control and *E12*<sup>-/-</sup> H1299 cell lines. Statistical significance was determined using Student's t-test.

For A-B. Data presented as mean  $\pm$  SEM. n = 3 independent experiments. \*\* p < 0.01, \*\*\* p < 0.001.

**A****B**

**Figure S3. *SCD1* transcript counts are increased in certain cancer types.**

A-B. *SCD1* transcript counts in the indicated tumors (data from TCGA) and the matched normal tissues (data from TCGA and GTEx) were analyzed via Gene Expression Profiling Interactive Analysis (GEPIA, <http://gepia.cancer-pku.cn/index.html>). \*\*\* p < 0.001.

**Table S1.** Primers used to generate expression vectors.

Name	Oligonucleotide	Sequence
p73-E12-gRNA-1- pSpCas9(BB)-2A-Puro	Sense	5`-CACCGCGTCACATCGCCAGGCCTT-3`
	Antisense	5`-AAACAAGGCCTGGCGATGTGACGC-3`
p73-E12-gRNA-2- pSpCas9(BB)-2A-Puro	Sense	5`-CACCGCTGCTGCTCATCTCGCCGT-3`
	Antisense	5`-AAACACGGCGAGATGAGCAGCAGC-3`

**Table S2.** Primers used for qPCR and ChIP.

<i>TP73<math>\alpha</math>1</i>	Sense	5`-CACCGTCAAACGTGGTGCCCCCATC-3`
	Antisense	5`-AAACGATGGGGGCACCACGTTTGAC-3`
<i>SCD1</i>	Sense	5`-CACTTGGGAGCCCTGTATGG-3`
	Antisense	5`-TGAGCTCCTGCTGTTATGCC-3`
<i>PCYT1A</i>	Sense	5`-GAGTTGCAGCATGTGCCGA-3`
	Antisense	5`-GCATTGACCTTGGCTGAACA-3`
<i>CEPT1</i>	Sense	5`-GGCAGTGATTGGAGGACCAC-3`
	Antisense	5`-TGCCAACACCACCTGTGAAG-3`
<i>SMPD4</i>	Sense	5`-GACTCCCAGCCCCGGTGT-3`
	Antisense	5`-CCACTCGGAACACCATGAG-3`
<i>SLC44A1</i>	Sense	5`-GCAGAGCTCCAAACGAGAA-3`
	Antisense	5`-AGCCACAAATAAATCCCATCCC-3`
<i>HPRT1</i>	Sense	5`-CACCGCGTCACATCGCCAGGCCTT-3`
	Antisense	5`-AAACAAGGCCTGGCGATGTGACGC-3`
<i>SCD1</i> -ChIP	Sense	5`-TGCAGGGGTTTTTCGGAGTTT-3`
	Antisense	5`-TGAACGCCCTATTCCAGCCTTA-3`
<i>CDKN1A</i> -ChIP	Sense	5`-GGTCTGCTACTGTGTCCTCC-3`
	Antisense	5`-CATCTGAACAGAAATCCCAC-3`
<i>GAPDH</i> -ChIP	Sense	5`-AAAAGCGGGGAGAAAGTAGG-3`
	Antisense	5`-AAGAAGATGCGGCTGACTGT-3`