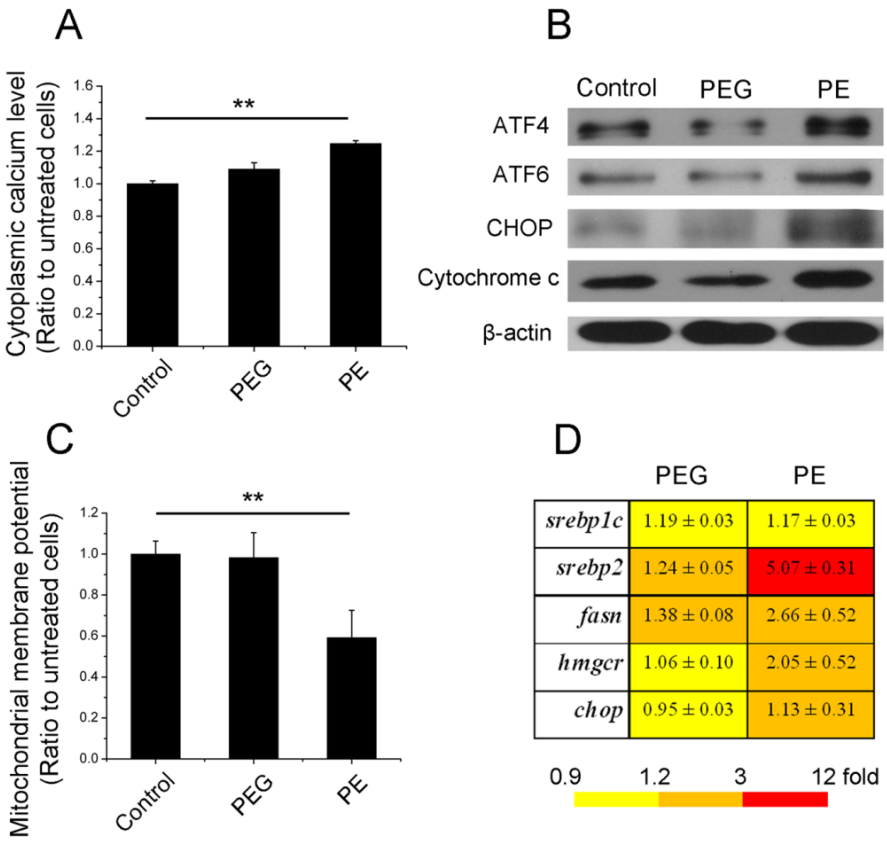

Figure S1. PE but not PEG induces ER membrane damage, UPR activation, lipid accumulation and mitochondrial membrane damage in A549 cancer cells. (A) Cytoplasmic calcium level, (B) expression of ATF4, ATF6, CHOP and cytochrome c protein, (C) mitochondrial membrane potential and (D) relative mRNA levels of lipid synthesis-related genes and *chop* in PEG-treated or PE-treated A549 cancer cells. Cells were incubated with 35 μM PEG or PE for 48 h. Untreated cells were taken as controls. PEG: poly(ethylene glycol); PE: phosphoethanolamine.

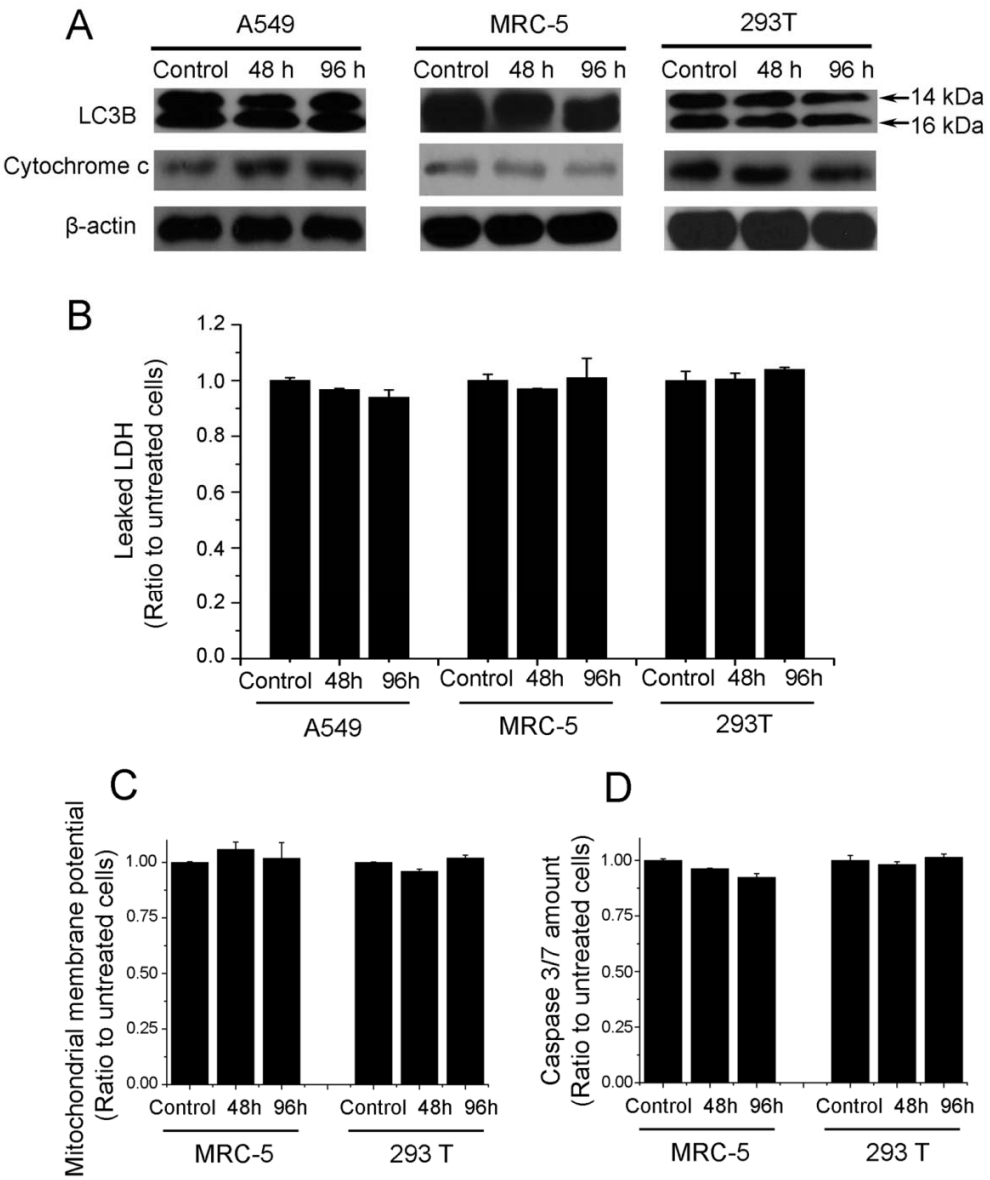

Figure S2. Cell viability of MRC-5 cells and 293T cells is not affected by PEG-PE. (A) Expression of LC3B and cytochrome c, (B) amount of extracellular lactate dehydrogenase (LDH), (C) mitochondrial membrane potential, and (D) amount of caspase-3/7 in PEG-PE-treated A549 cancer cells, and MRC-5 cells and 293T cells. Cells were incubated with 35 μM PEG-PE micelles for 48 h or 96 h. Untreated cells were taken as controls.

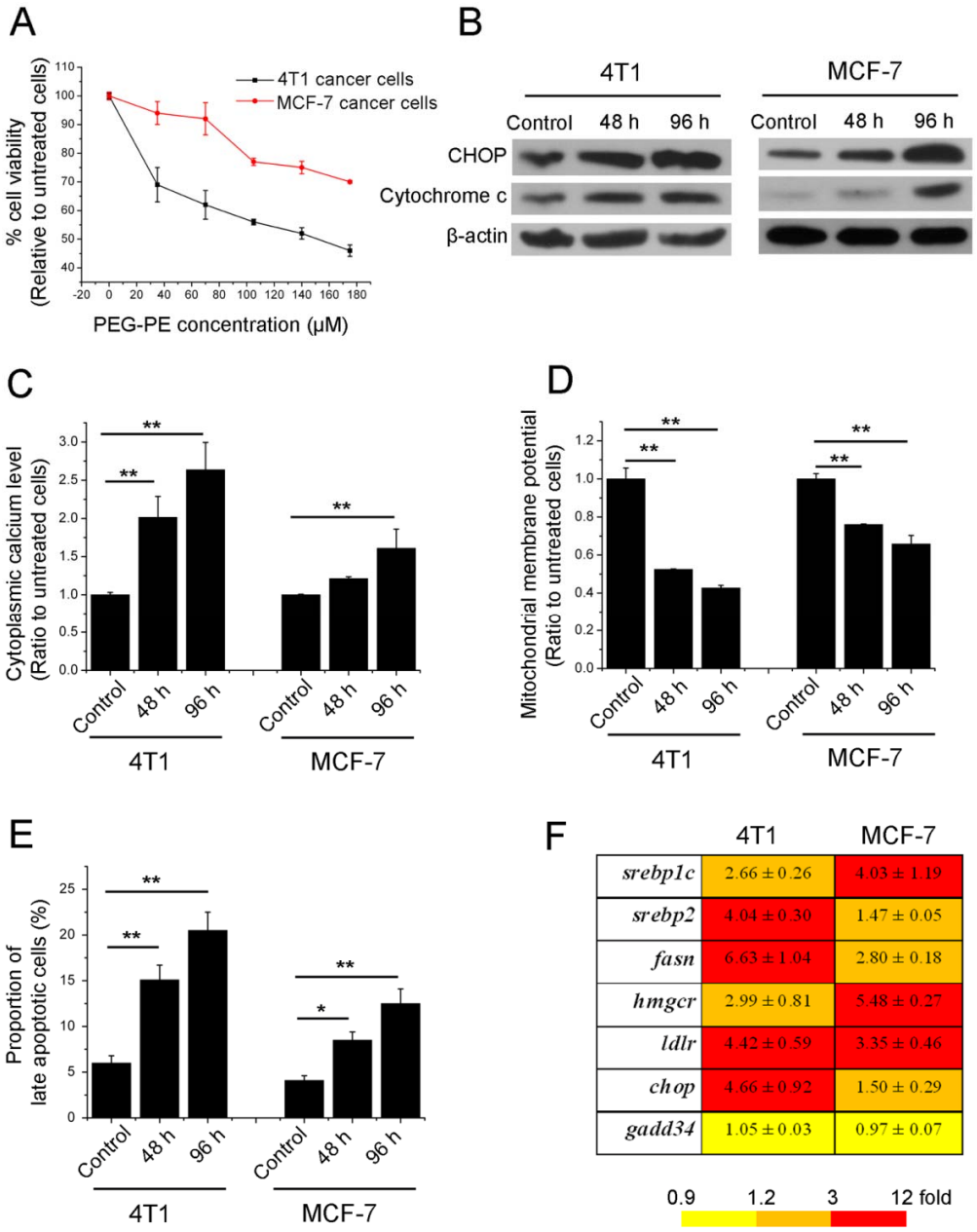

Figure S3. PEG-PE induces ER stress, apoptosis and lipid accumulation in 4T1 cancer cells and MCF-7 cancer cells. (A) Cell viability, (B) expression of CHOP and cytochrome c protein, (C) cytoplasmic calcium level, (D) mitochondrial membrane potential, (E) Annexin V / PI analysis, and (F) relative mRNA levels of lipid synthesis-related genes, *chop* and *gadd34* in PEG-PE-treated 4T1 and MCF-7 cancer cells. Cells were incubated with 35 μM PEG-PE micelles for 48 h or 96 h. Untreated cells were taken as controls.

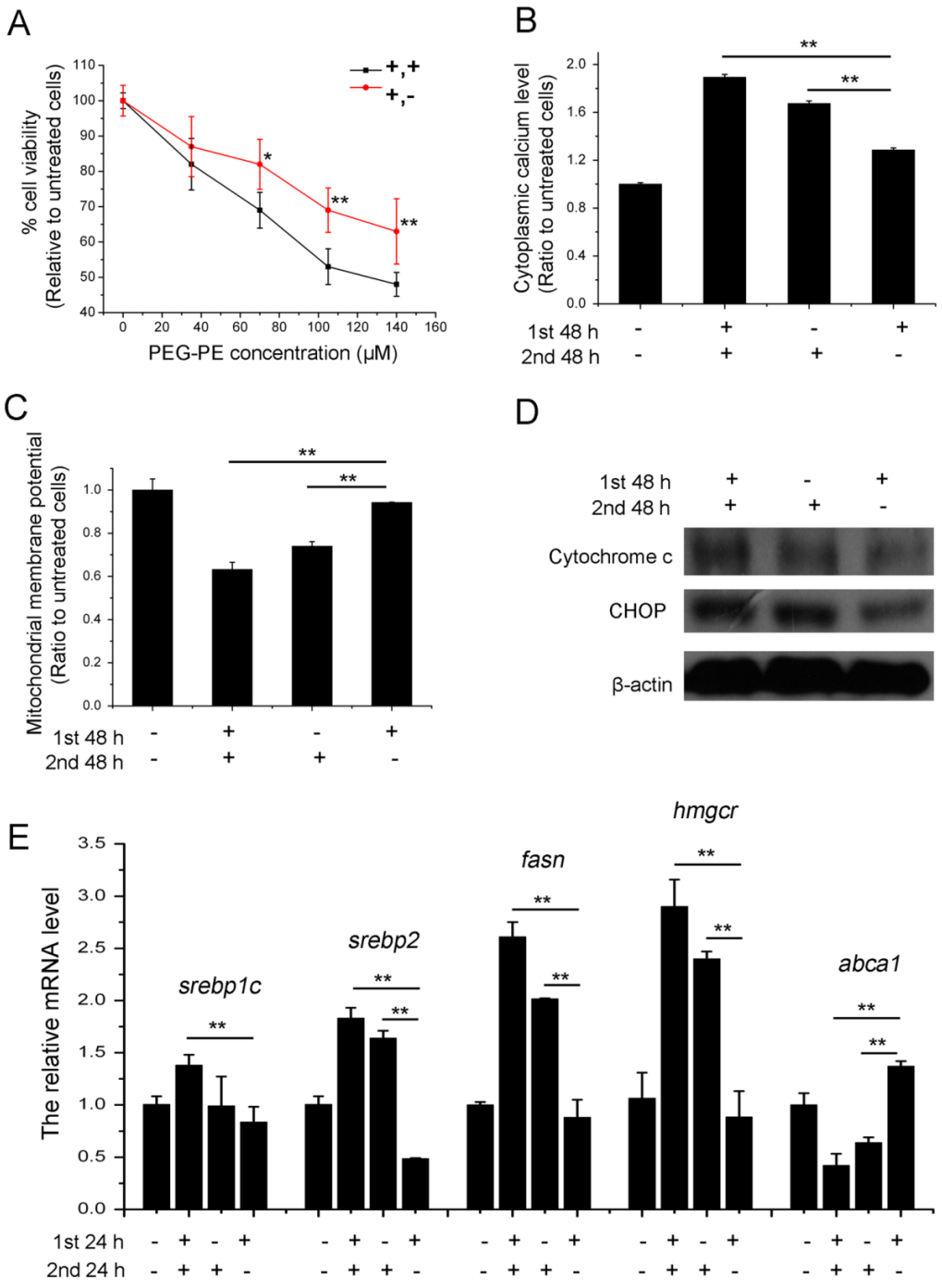

Figure S4. A549 cancer cells can partially recover from PEG-PE-induced ER stress. (A) Cell viability of A549 cancer cells incubated with 35 μM PEG-PE micelles for 96 h (indicated by +, +), or treated with micelles for the first 48 h and then incubated in micelle-free medium for the next 48 h (indicated by +, -). (B) Cytoplasmic calcium level, (C) mitochondrial membrane potential, (D) expression of CHOP and cytochrome c protein, and (E) relative mRNA levels of lipid synthesis-related genes in

untreated A549 cancer cells (indicated by -,-), or in cells treated with 35 μM PEG-PE micelles for the full 96 h (or 48 h) (indicated by +,+), or for the latter 48 h (or 24 h) (indicated by -,+), or for the former 48 h (or 24 h) and then incubated in micelle-free medium for another 48 h (or 24 h) (indicated by +,-).

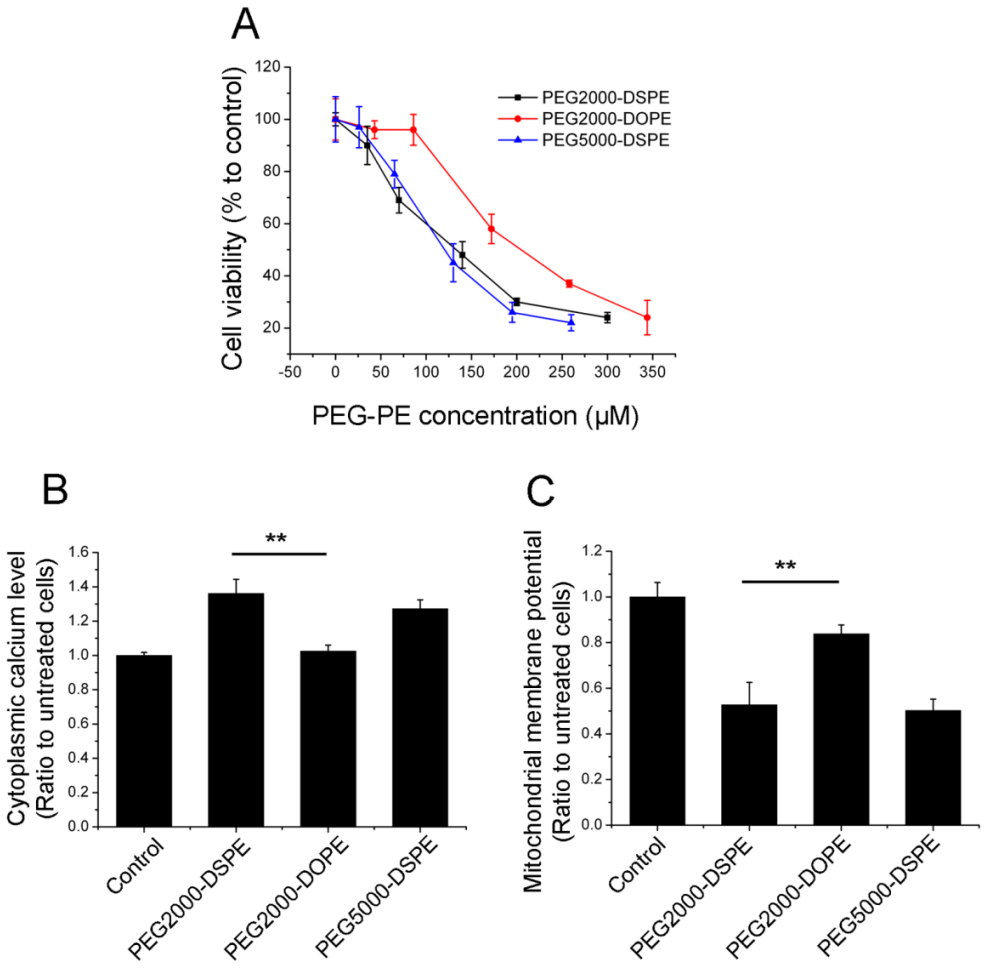

Figure S5. PEG2000-DSPE has a similar level of cytotoxicity to PEG5000-DSPE, but is more toxic than PEG2000-DOPE. (A) Cell viability, (B) cytoplasmic calcium level and (C) mitochondrial membrane potential of A549 cancer cells after incubation with different kinds of PEG-PE micelles for 48 h. In (B) and (C), cells were treated with 35 μM PEG-PE micelles.

Supporting Table 1. The primers for different genes.

Gene	Forward sequence	Reverse sequence
srebp1c	ACTTCCCTGGCCTATTTGACC	GGCATGGACGGGTACATCTT
srebp2	CGACGAGATGCTGCAATTTGT	CAGGGAACTCTCCCACTTGAT
acaca	ATGTCTGGCTTGCACCTAGTA	CCCCAAAGCGAGTAACAAATTCT
fasn	TGTGGACATGGTCACGGAC	GGCATCAAACCTAGACAGGTC
scd	TCTAGCTCCTATACCACCACCA	TGTCGTCTTCCAAGTAGAGGG
gpam	GATGTAAGCACACAAGTGAGGA	TCCGACTCATTAGGCTTTCTTTC
hmgcs	GATGTGGGAATTGTTGCCCTT	ATTGTCTCTGTTCCAACTTCCAG
hmgcr	GGACCCCTTTGCTTAGATGAAA	CCACCAAGACCTATTGCTCTG
fdps	AGGTGGCTGGGTTCCCTAC	TCTGGTCTCCGTTCATTCTGA
fdft1	ATGGAGTTCGTGAAATGCCTT	TGCGACTGGTCTGATTGAGATA
ldlr	TCGGGATCCTGACACTCAT	GAATATGACTGCAAGGACATGAGC
abca1	AACTCTACATCTCCCTTCCCG	CTCCTGTCGCATGTCACTCC
bcl-2	GGGGAGGATTGTGGCCTTC	CAGGGCGATGTTGTCCACC
bcl-xl	GGTCGCATTGTGGCCTTTTTC	TGCTGCATTGTTCCCATAGAG
bax	GGGTGGTTGGGTGAGACTC	AGACACGTAAGGAAAACGCATTA
bak	GTTTTCCGCAGCTACGTTTTT	GCAGAGGTAAGGTGACCATCTC
ero1l	GGCTGGGGATTCTTGTTTGG	AGTAACCACTAACCTGGCAGA
ero1l b	TTCTGGATGATTGCTTGTGTGAT	GGTCGCTTCAGATTAACCTTGT
chop	CAAGAGGTCCTGTCTTCAGATGA	TCTGTTTCCGTTTCCTGGTTC
gadd34	ATGATGGCATGTATGGTGAGC	AACCTTGCAGTGTCCTTATCAG

srebp: sterol regulatory element-binding protein; *acaca*: acetyl-CoA carboxylase; *fasn*: fatty acid synthase; *scd*: steatoyl-CoA desaturase; *gpam*: glycerol-3-phosphate acyltransferase; *hmgcs*: HMG-CoA synthase; *hmgcr*: HMG-CoA reductase; *fdps*: farnesyl diphosphate synthase; *fdft1*: farnesyl-diphosphate farnesyltransferase 1; *ldlr*: low-density lipoprotein receptor. *ero*: endoplasmic reticulum oxidase; *abca1*: ATP-binding cassette transporter A1; *chop/gadd153*: C/EBP-homologous protein / growth-arrest and DNA-damage inducible protein 153; *gadd34*: growth-arrest and DNA-damage inducible protein 34.