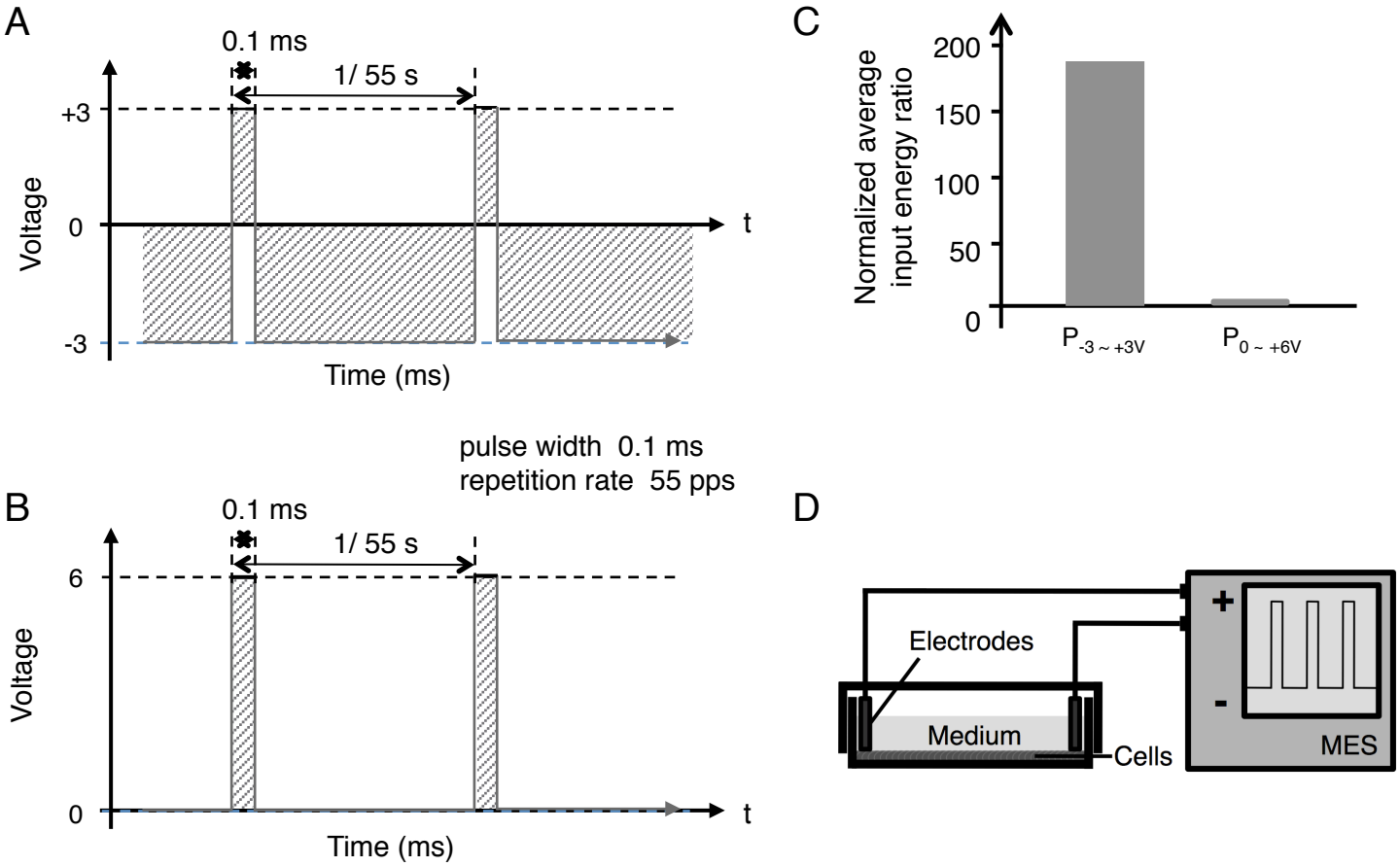
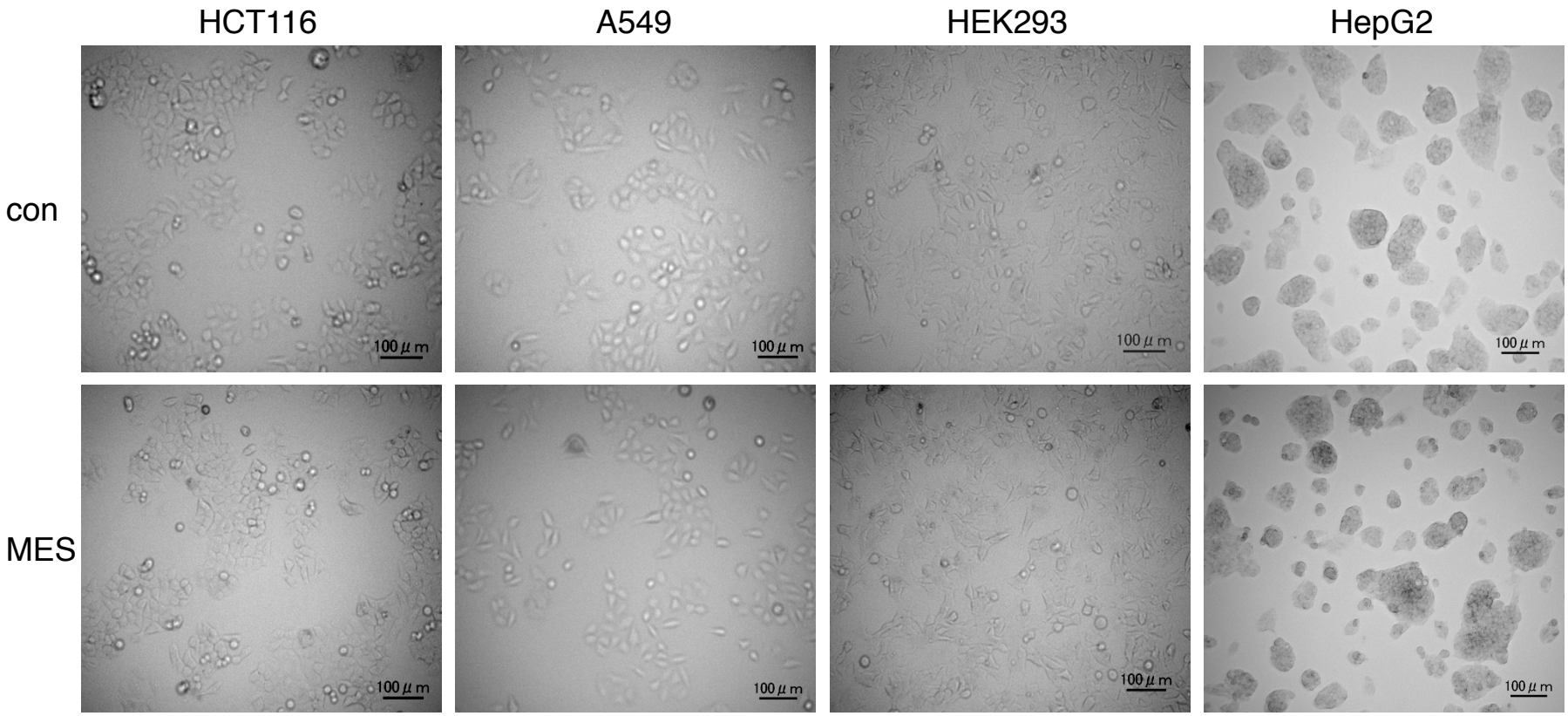
Supplemental Figure S1



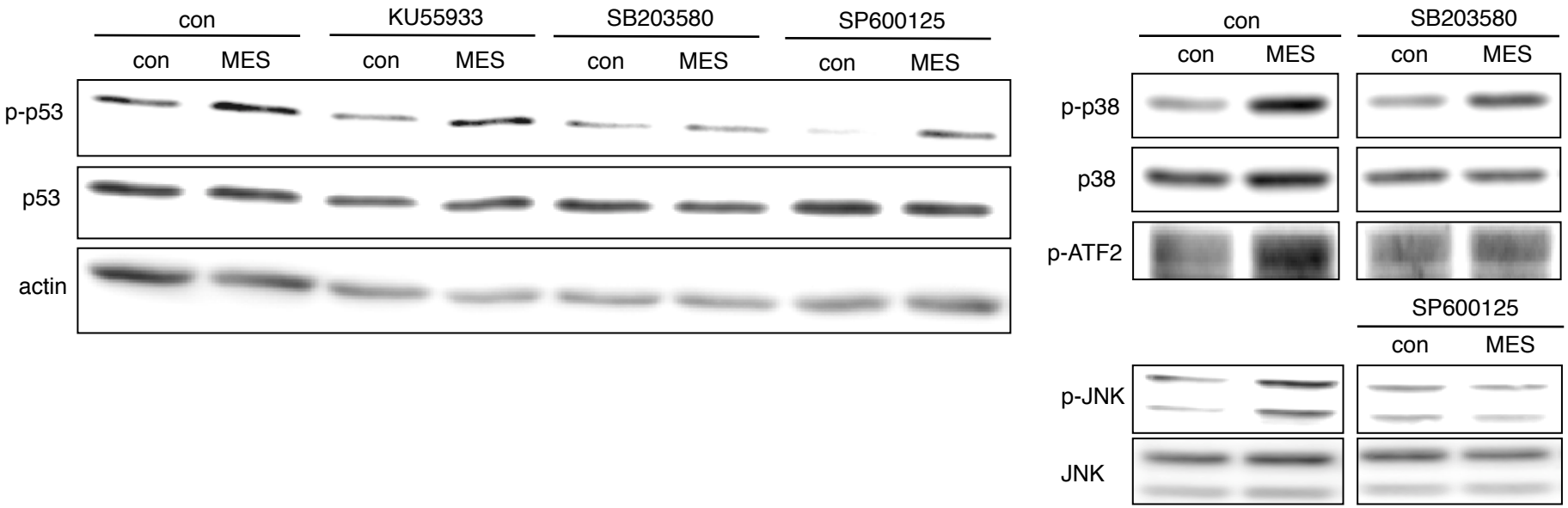
The average input energy varies with the reference voltage.
(A, B) The schematic of voltage waveform of 6 V amplitude with the reference voltage. (A) V_0 = -3 V; (B) V_0 = 0 V (C) The normalized average input energy of reference voltage (-3 or 0). Pulse width 0.1 ms; Repetition rate 55 pps.Average input energy, P, is $P= W/t = VI$ where W is Total input energy, t is time, V is voltage, I is ampere. Because the average input energy, P, depends on the voltage, P depends on the hatched area (A, B). (D) Diagram of apparatus for MES treatment.

Supplemental Figure S2



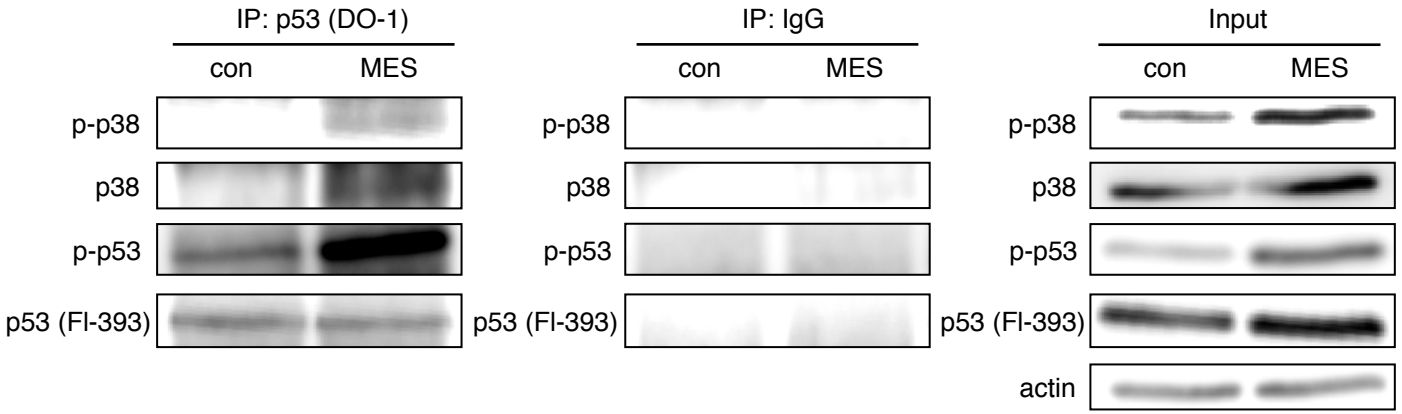
MES treatment does not affect cellular morphology.
HCT116, A549, HepG2 and HEK293 cells were treated with MES (1 V/cm, 0.1 ms, 55 pps) for 10 min. One hour after MES treatment, cell morphology was visually assessed using confocal microscope.

Supplemental Figure S3



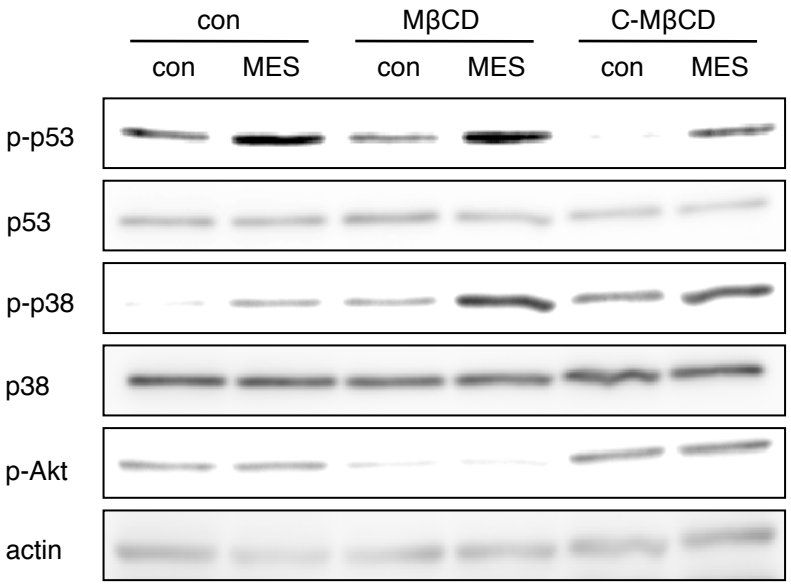
MES-induced p53 phosphorylation is not mediated by JNK or ATM pathways.
HCT116 cells were treated with ATM pathway inhibitor, KU55933 (10 μM; #118500; Calbiochem), p38 pathway inhibitor, SB203580 (10 μM; Calbiochem) or JNK pathway inhibitor, SP600125 (20 μM; #BML-EI305; Enzo Life Science) for 1 hr before treatment with MES (1 V/cm, 0.1 ms, 55 pps) for 30 min. Cell lysates were extracted 1 hr after MES treatment, and analyzed by Western blotting using the indicated antibodies. Phospho-JNK (Thr-183 and Tyr-185) and JNK were from Cell Signaling Technology. Actin served as loading control.

Supplemental Figure S4



MES increases p-p38-p53 interaction.
HCT116 cells were cross-linked 1 hr after MES treatment. Protein lysates were immunoprecipitated with p53 (DO-1) antibody or mouse IgG-conjugated magnetic beads (#DB10003, VERITAS). Immunoprecipitated lysates and input samples were immunoblotted and analyzed using the indicated antibodies.

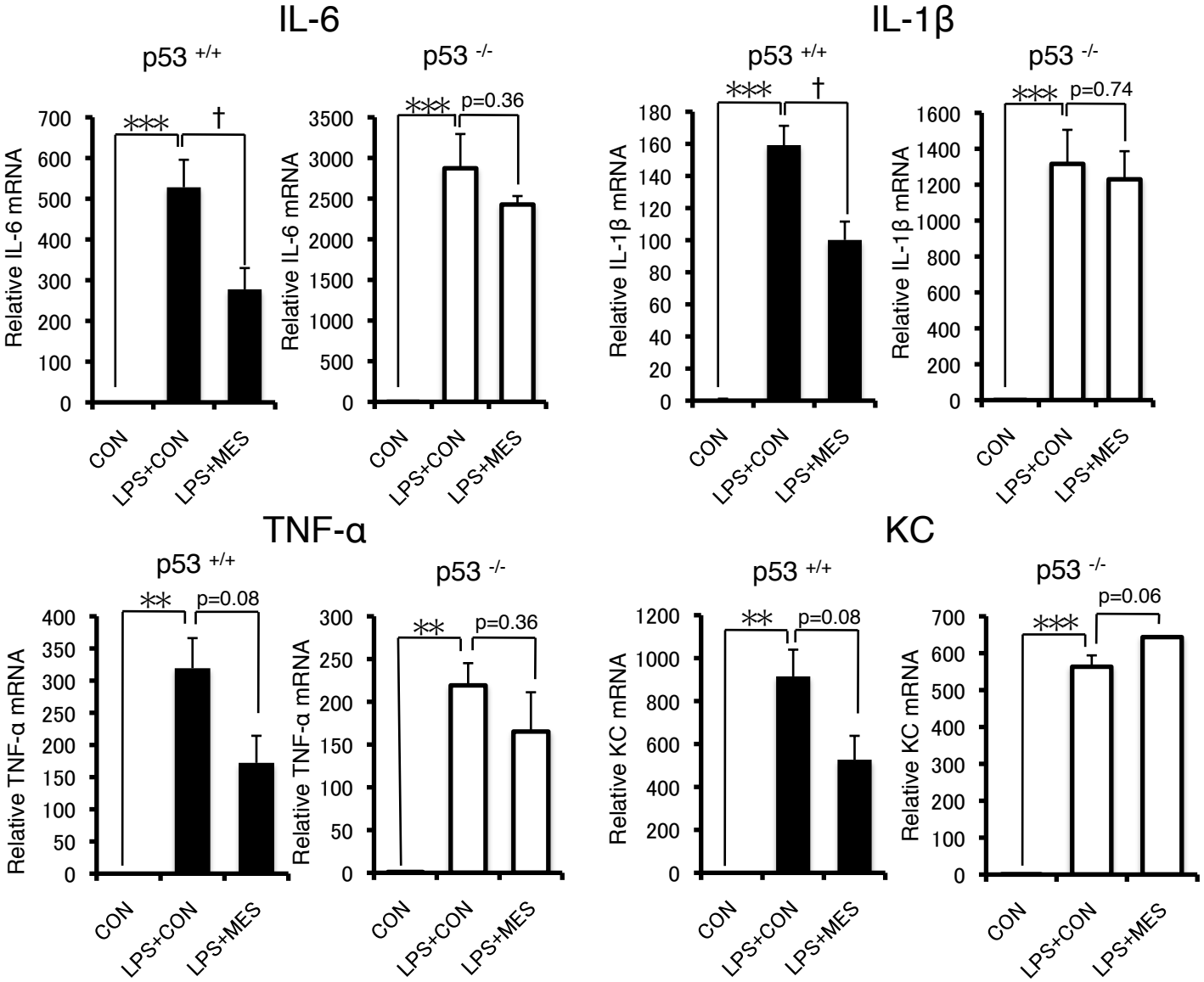
Supplemental Figure S5



Cholesterol ablation has no effect on activation of p38-p53 signaling by MES in HCT116 cells.

HCT116 cells were depleted of lipid raft by incubation with 10 mM methyl-β-cyclodextrin (MβCD) or cholesterol-saturated MβCD (C-MβCD) for 30 min, and were treated with MES (0.1 ms, 1 V/cm, 55 pps) for 30 min in the presence of 10 mM MβCD or C-MβCD. One hour after MES treatment, cell lysates were extracted. p-Akt was used as control of cholesterol depletion. Actin served as internal control.

Supplemental Figure S6



MES attenuates LPS-induced inflammatory cytokine response dependently on p53 in peritoneal macrophages.
$p53^{+/+}$ or $p53^{-/-}$ mouse-derived peritoneal macrophages were pre-treated with MES (1 V/cm, 0.1 ms, 55 pps) for 30min and stimulated with 0.01μg/ml of lipopolysaccharide (LPS) for 4hr. Total RNA was extracted after LPS treatment and mRNA expression levels of IL-6, IL-1β, TNF-α and KC (mouse IL-8) were analyzed by quantitative real-time PCR. GAPDH was used as internal control. The experiments were performed in triplicate. Bars indicate the mean ± SE. **P<0.01, ***P<0.001 vs control, †P<0.05 vs LPS+CON, assessed by Student's t-test.

Supplemental Table S1

Primers used for quantitative PCR in Supplemental Figure S6.

Primer name	Forward	Reverse
mouse IL-6	5'-GAGGATACCACTCCCAACAGACC -3'	5'-AAGTGCATCATCGTTGTTCATACA-3'
mouse IL-1β	5'-GCTGAAAGCTCTCCACCTCAATG -3'	5'-TGTCGTTGCTTGGTTCTCCTTG -3'
mouse TNF-α	5'-CATCTTCTCAAAATTCGAGTGACAA -3'	5'-TGGGAGTAGACAAGGTACAACCC -3'
mouse IL-8 (KC)	5'-TGTCAGTGCCTGCAGACCAT -3'	5'-GAGCCTTAGTTTGGACAGGATCTG -3'
mouse GAPDH	5'-CCTGGAGAAACCTGCCAAGTATG -3'	5'-GGTCCTCAGTGTAGCCCAAGATG -3'