Supplementary figure legends

Figure S1. SPD increases NRF2 via autophagic degradation of KEAP1. A-B. Whole western blot image of p62 and KEAP1 in Figure 1A (A) and Figure1B (B). C-D. quantification of western blots from Figure 1A (C) and Figure 1B (D). Results are expressed as mean ± SD. *: $p < 0.05$ compared with the control group.

Figure S2. CYP2E1 levels are not affected by genotype. A-B. Immunoblot analysis of CYP2E1 protein levels in WT, *Nrf2*$^{-/-}$, *p62*$^{-/-}$ and *Nrf2*$^{-/-}$;*p62*$^{-/-}$ mice. GAPDH was used as an internal loading control. Results are expressed as mean ± SD. *: $p < 0.05$ compared with the control group.

Figure S3. IHC staining of liver tissue from WT, *Nrf2*$^{-/-}$, *p62*$^{-/-}$ and *Nrf2*$^{-/-}$;*p62*$^{-/-}$ mice. MAP1S (A), NRF2 (B), NQO1(C), FTL (D), 8-oxo-deoxyguanosine (8-oxo-dG) (E) and p62 (F) were subjected to IHC analysis. The quantification of each staining is shown in the lower panel. Results are expressed as mean ± SD. A Student's unpaired t-test was used to compare, and $p < 0.05$ was considered statistically significant. *: $p < 0.05$ compared between different groups. Scale bar=50 μm.

Figure S4. Isolation of HSCs from liver tissue. A. Phase contrast image of HSCs from each indicated genotype. B. IF staining for glial fibrillary acidic protein (GFAP) was used as an HSC marker. Scale bar=100 μm.

Figure S1

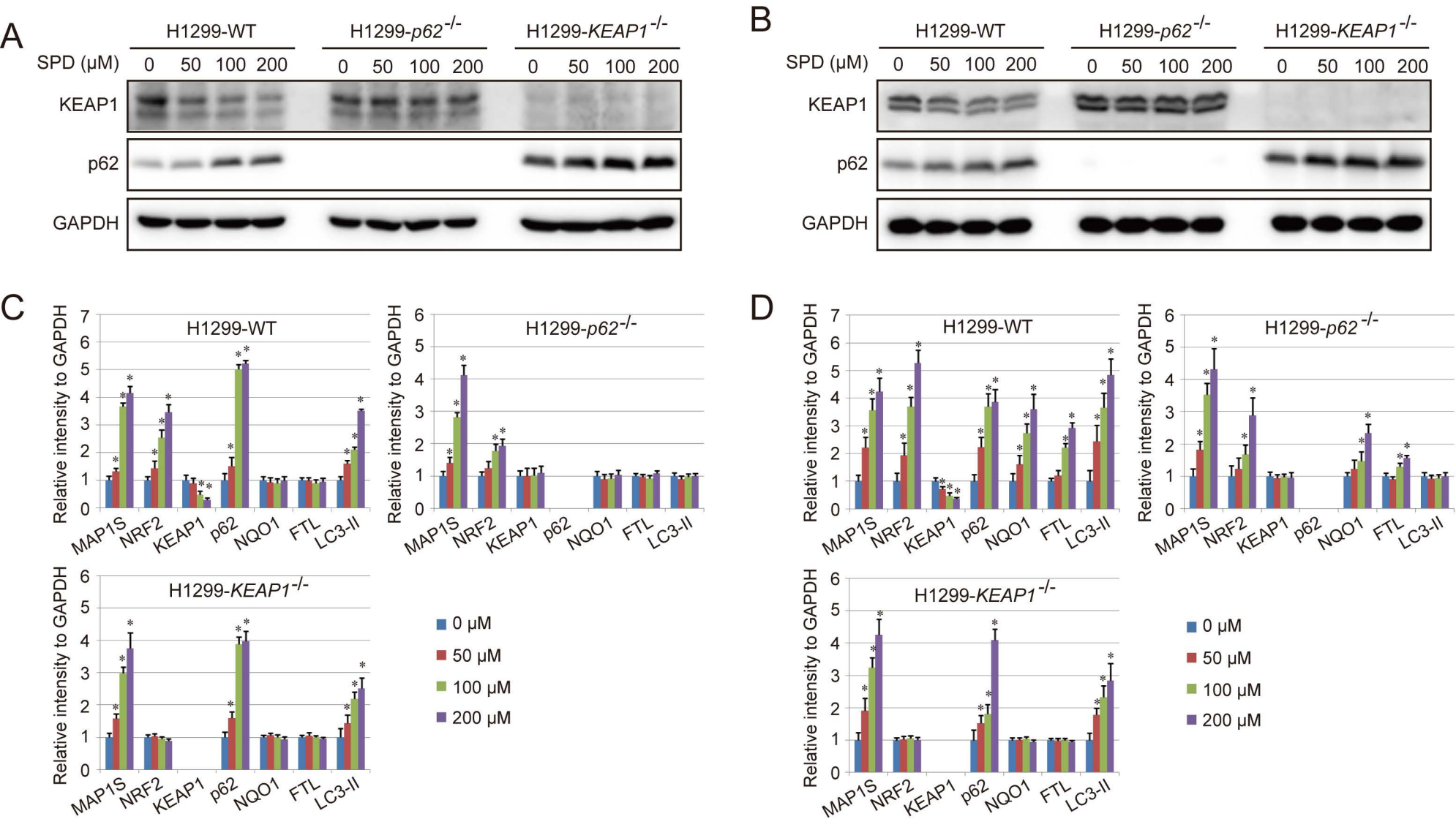
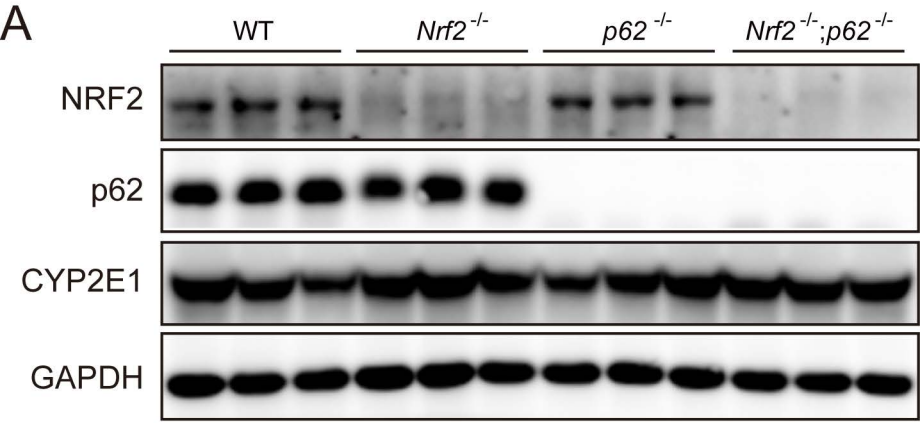

A
H1299-WT
H1299-p62-/-
H1299-KEAP1-/-
SPD (μM)
0 50 100 200
KEAP1
p62
GAPDH
B
C
D
Relative intensity to GAPDH
MAP1S NRF2 KEAP1 p62 NQO1 FTL LC3-II
0 μM
50 μM
100 μM
200 μM

Figure S2


A
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
NRF2
p62
CYP2E1
GAPDH

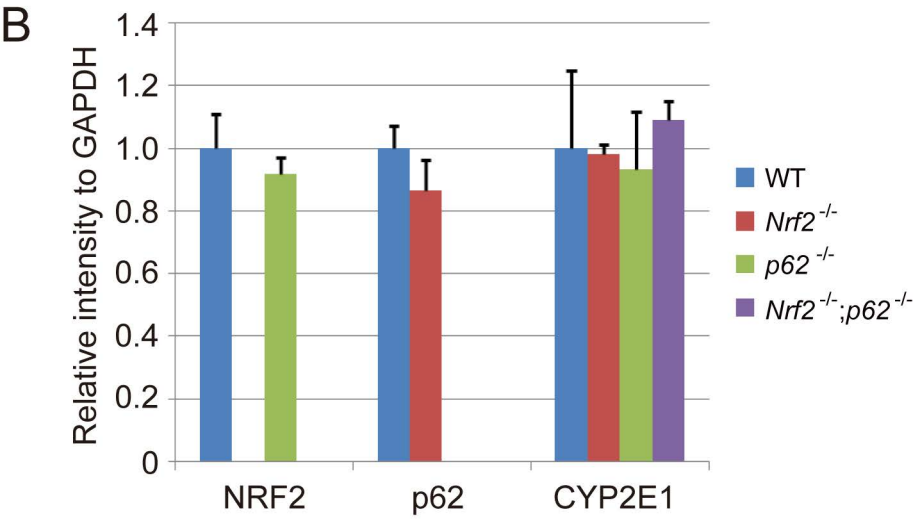
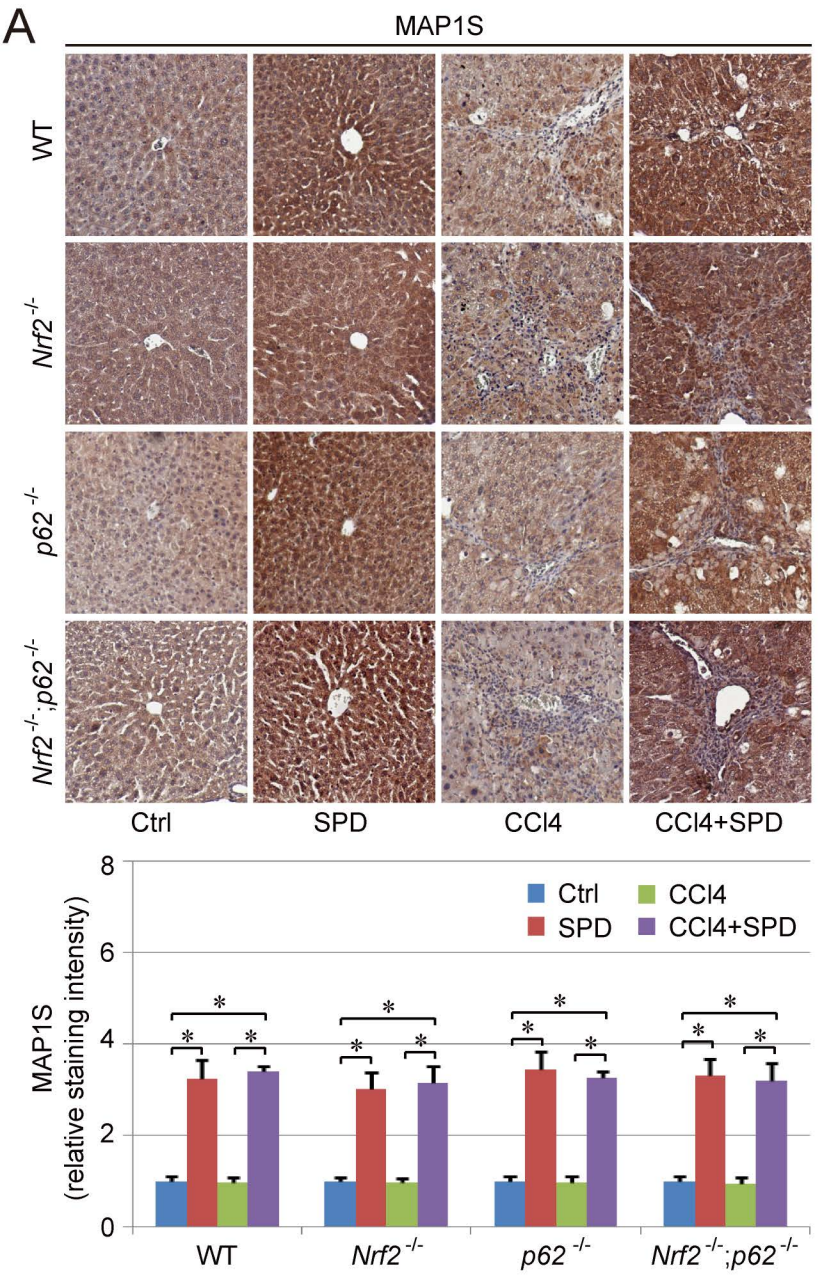
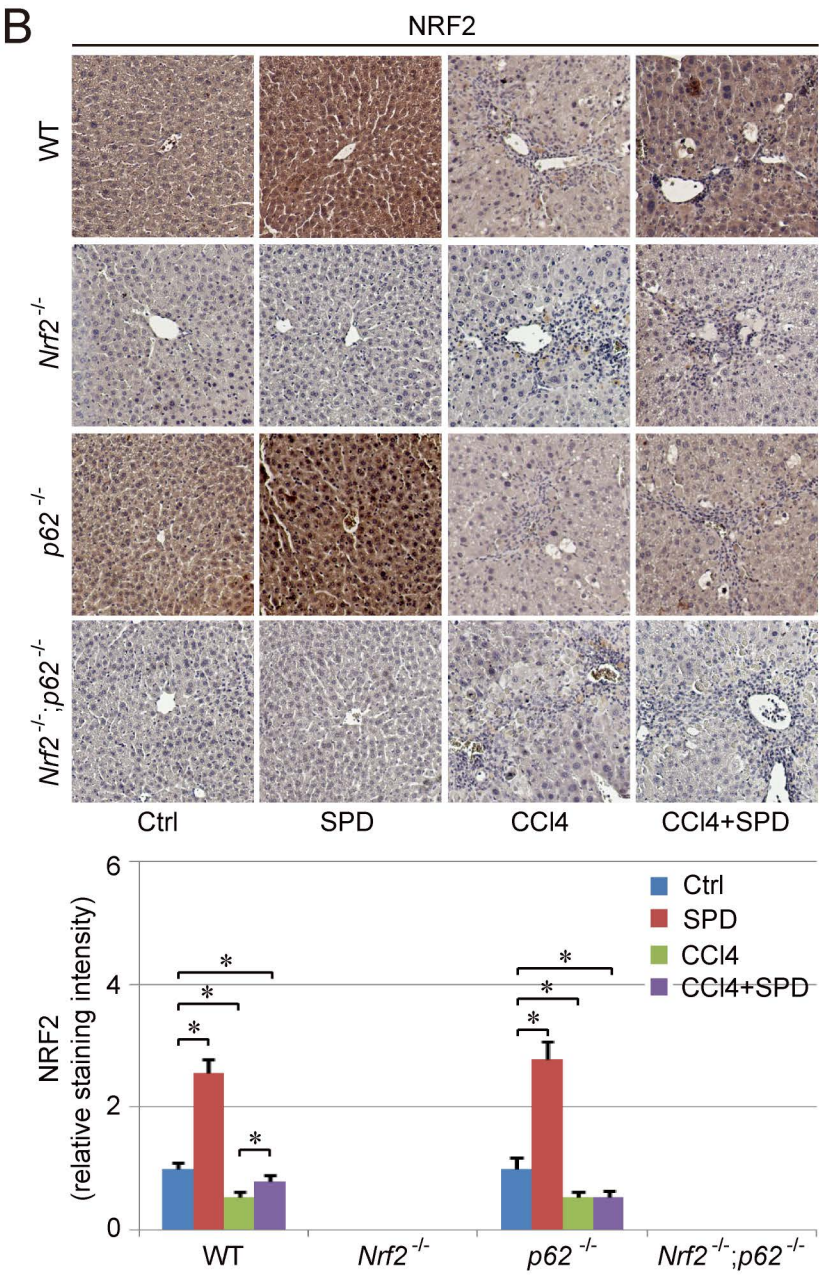
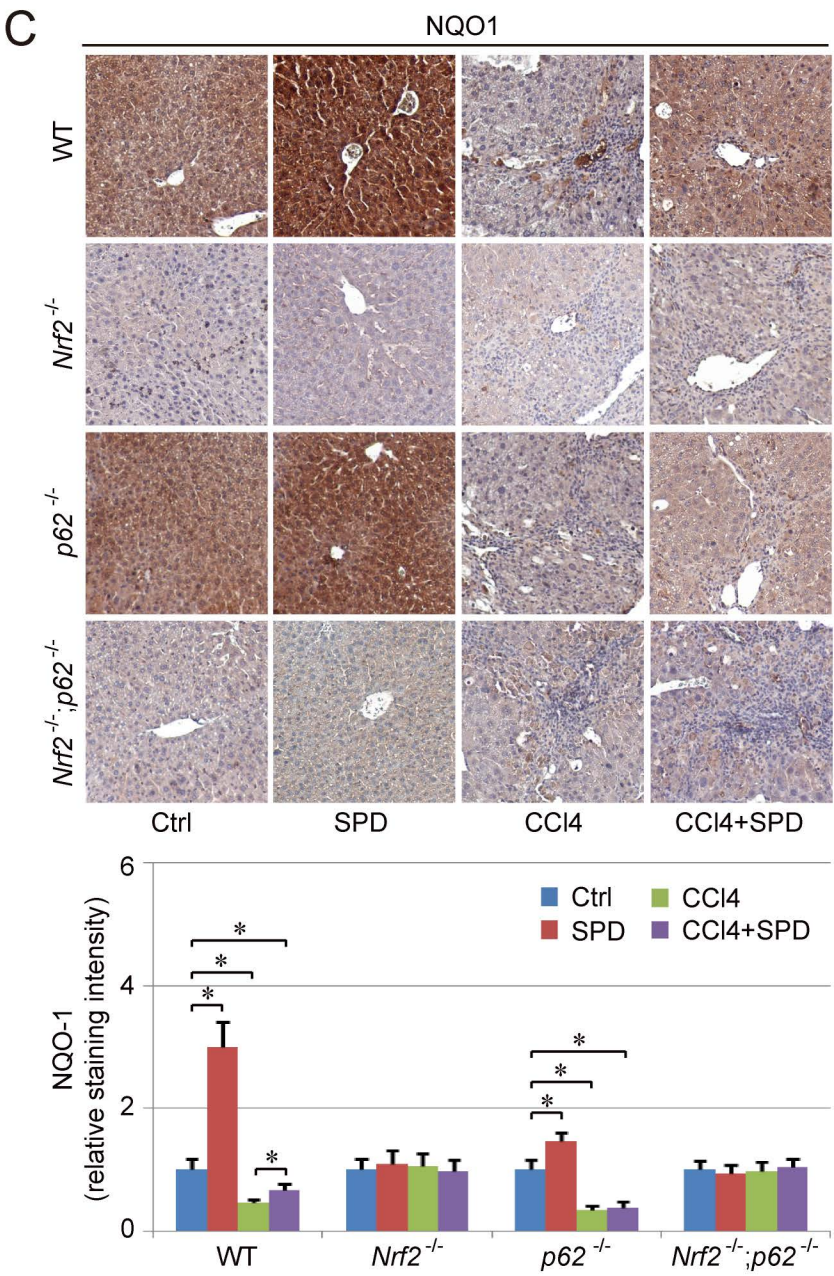
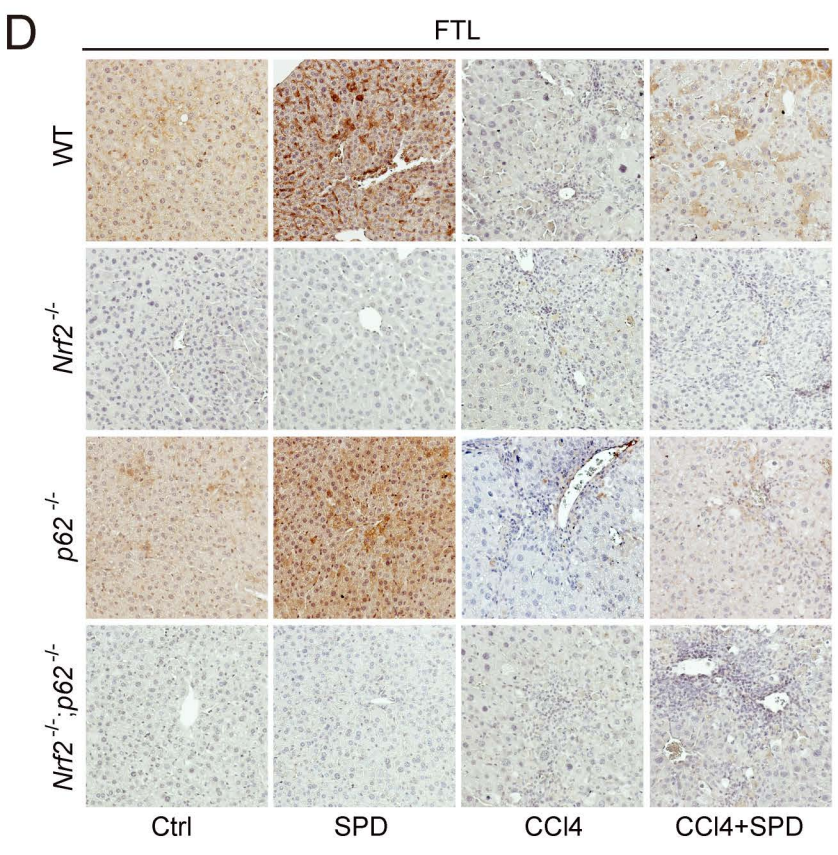

B
Relative intensity to GAPDH
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
NRF2
p62
CYP2E1
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-

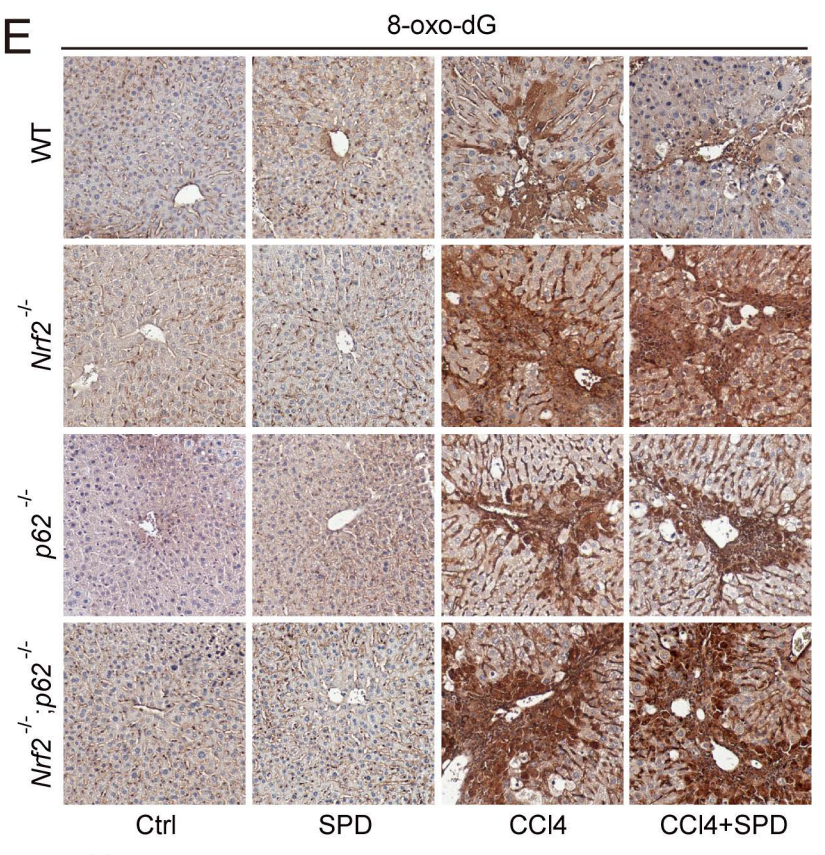
Figure S3


A
MAP1S
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
MAP1S (relative staining intensity)
0
2
4
6
8
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-


B
NRF2
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
NRF2 (relative staining intensity)
0
2
4
6
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-


C
NQO1
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
NQO-1 (relative staining intensity)
0
2
4
6
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-


D
FTL
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
FTL (relative staining intensity)
0
2
4
6
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-


E
8-oxo-dG
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
8-oxo-dG (relative staining intensity)
0
5
10
15
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-

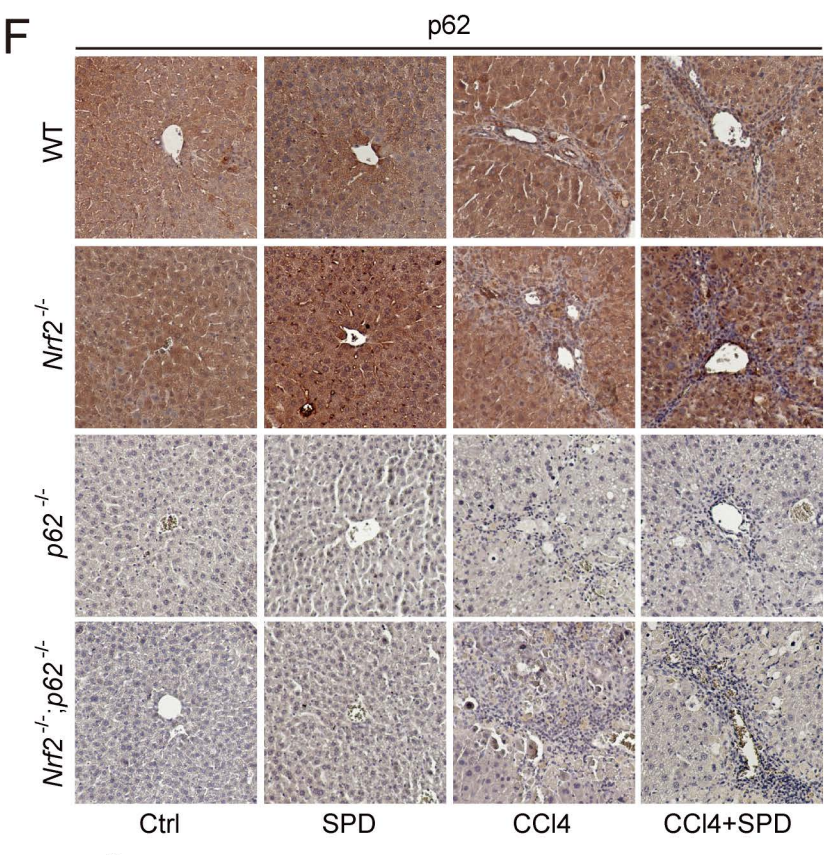
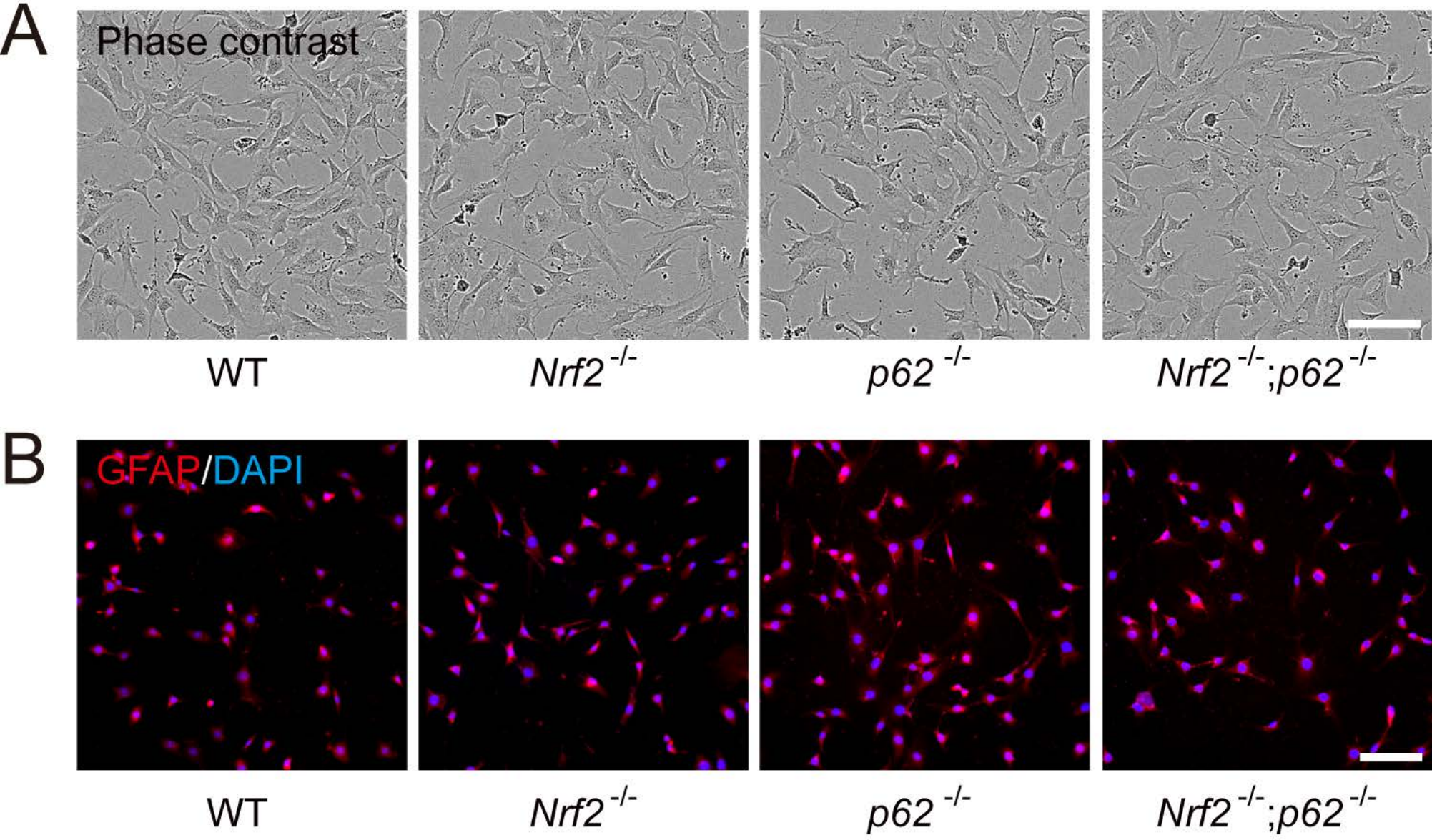

F
p62
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
Ctrl
SPD
CCl4
CCl4+SPD
p62 (relative staining intensity)
0
1
2
3
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-

Figure S4


A
Phase contrast
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-
B
GFAP/DAPI
WT
Nrf2 -/-
p62 -/-
Nrf2 -/-;p62 -/-