

Supplementary materials

Supplementary Figure 1. The mRNA level of *Blt1*, *Blt2* and *Cysltr2* in mice liver after acute APAP administration.

C57BL/6J mice fasted overnight, then were orally administered with saline or APAP (200 mg/kg) for 12 hours. The hepatic mRNA expression of *Blt1*, *Blt2* and *Cysltr2* were detected by RT-qPCR analysis. Data are mean \pm SEM, n = 5 for saline group, n=6 for APAP group. * $P < 0.05$.

Supplementary Figure 2. APAP treatment upregulated *Cysltr1* expression *in vivo*.

A-B, Primary hepatocytes were treated with vehicle or APAP (2.5 mM) for 24 hours. The mRNA levels of *Cysltr1*, *Cysltr2*, *Blt1* and *Blt2* in primary hepatocytes were detected by RT-qPCR analysis. Data are mean \pm SEM, n = 5 for each group, * $p < 0.05$. **C**, Western blot analysis of *Cysltr1*. Primary hepatocytes were treated with 2.5 mM APAP for 0, 3, 8 or 24 hours. **D**, Quantification of *Cysltr1* to β -actin. Data are mean \pm SEM, n = 5, * $p < 0.05$. Experiments were repeated 3 times with similar results.

Supplementary Figure 3. Montelukast administration did not affect APAP phase I/II metabolizing enzymes.

A-C, The hepatic mRNA levels of *Cyp1a2*, *Cyp 2a1*, and *Cyp3a11*. **D-E**, The mRNA levels of *Ugt1a1* and *Sult2a1*. Data are mean \pm SEM, n = 5 for saline groups, n = 7 for APAP groups.

Supplementary Figure 4. The hepatic mRNA levels of transporters and GSTs.

A-C, The expression of *Mrp2*, *Mrp3* and *Mrp4*. **D-F**, The hepatic mRNA levels of *GSTa1*, *GSTM1*, and *GSTM2*. Data are mean \pm SEM, n = 5 for saline groups, n = 7 for APAP groups.

Supplementary Figure 5. Montelukast inhibit *Cysltr1* expression in APAP-treated hepatocytes.

A, Primary hepatocytes were pretreated with montelukast (1, 5 and 10 μ M) or vehicle (DMSO) 1 hour before APAP (2.5 mM) administration. Quantification of LDH released into the culture medium of primary hepatocyte after treatment with 2.5 mM of APAP for 24 hours. Data are mean \pm SEM, n=3 for each group, ** $p < 0.01$. **B**, Primary hepatocytes were pretreated with montelukast (5 μ M) or vehicle (DMSO) 1 hour before APAP (2.5 mM) administration. Western blot analysis of *Cysltr1*. Experiments were repeated 3 times with similar results.

Supplementary Figure 6. Zafirlukast inhibit APAP-induced cell damage.

A-B, Primary hepatocytes were pretreated with zafirlukast (5 μ M) or vehicle (DMSO) 1 hour before APAP (2.5 mM) administration. **A**, Quantification of LDH released into the culture medium of primary hepatocyte after treatment with 2.5 mM of APAP for 24 hours. Data are mean \pm SEM, n = 3 for each group, ** $p < 0.01$. **B**, Primary hepatocytes were incubated with 5mg/L JC-1 dye for 30 min at 37°C in the dark and washed twice with the dye buffer. Then the cells were quickly subjected to fluorescence microscope for captured red or green fluorescence. Experiments were repeated 3 times with similar results.

Supplementary Figure 7. Montelukast inhibit LTD₄-induced cell death.

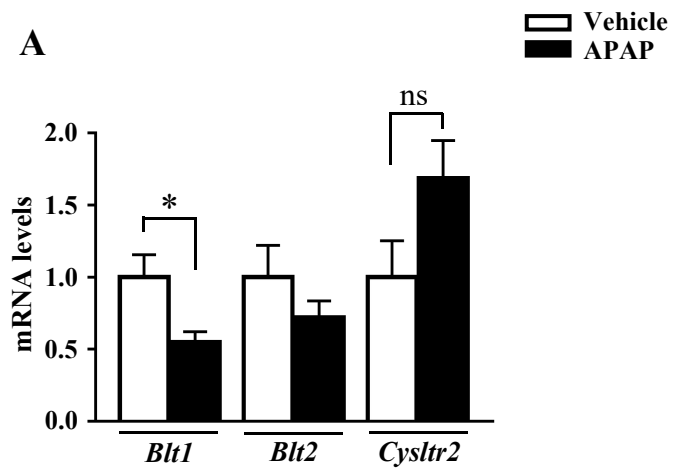
A-C, Primary hepatocytes were pretreated with montelukast (5 μ M) or vehicle (DMSO) 1 hour before LTD₄ (100 nM) administration. **A**, Representative morphological images of primary hepatocytes treated with LTD₄ for 24 hours. **B**, Quantification of LDH released into the culture medium of primary

hepatocyte after treatment with 2.5 mM of APAP for 24 hours. Data are mean \pm SEM, n = 3 for each group. * p < 0.05. C, Primary hepatocytes were incubated with 5mg/L JC-1 dye for 30 min at 37°C in the dark and washed twice with the dye buffer. Then the cells were quickly subjected to fluorescence microscope for captured red or green fluorescence. Experiments were repeated 3 times with similar results.

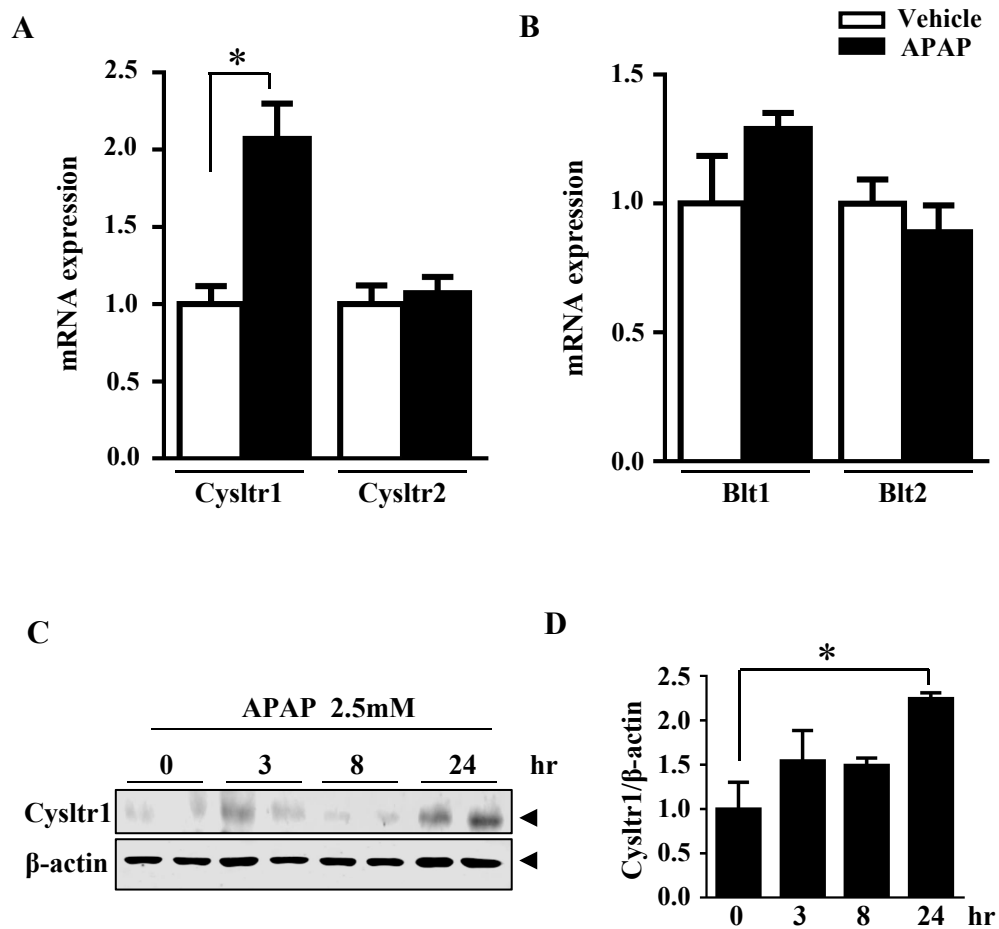
Supplementary Table 1: List of specific primers used for real-time quantitative PCR

Genes	Forward sequence(5'-3')	Reverse sequence(5'-3')
<i>18s</i>	TTGACTCAACACGGGAAACC	AGACAAATCGCTCCACCAAC
<i>Blt1</i>	ATGGCTGCAAACACTACATCTC	GACCGTGCGTTTCTGCATC
<i>Blt2</i>	ATGTCTGTCTGCTACCGTCC	AGCTCCATACTACGAAGCCAT
<i>Cysltr1</i>	CCTCTCCGTGTGGTCTATTATGT	ATGCAAACGAACCTGGCTTTT
<i>Cysltr2</i>	TGTCACCAGTGTCAGGAGTG	ACTTTTGAGGACTCAGCTCCAA
<i>Mcp1</i>	GCTGGAGAGCTACAAGAGGATC	GTCAACTTCACATTCAAAGGTGC
<i>Tnf-α</i>	GGCGGTGCCTATGTCTCA	AGGGTCTGGGCCATAGAA
<i>Il-6</i>	TTCTTGGGACTGATGCTG	CTCATTTCACGATTTCCC
<i>Il-18</i>	CACATGCGCCTTGTGATGAC	TGCAGCCTCGGGTATTCTG

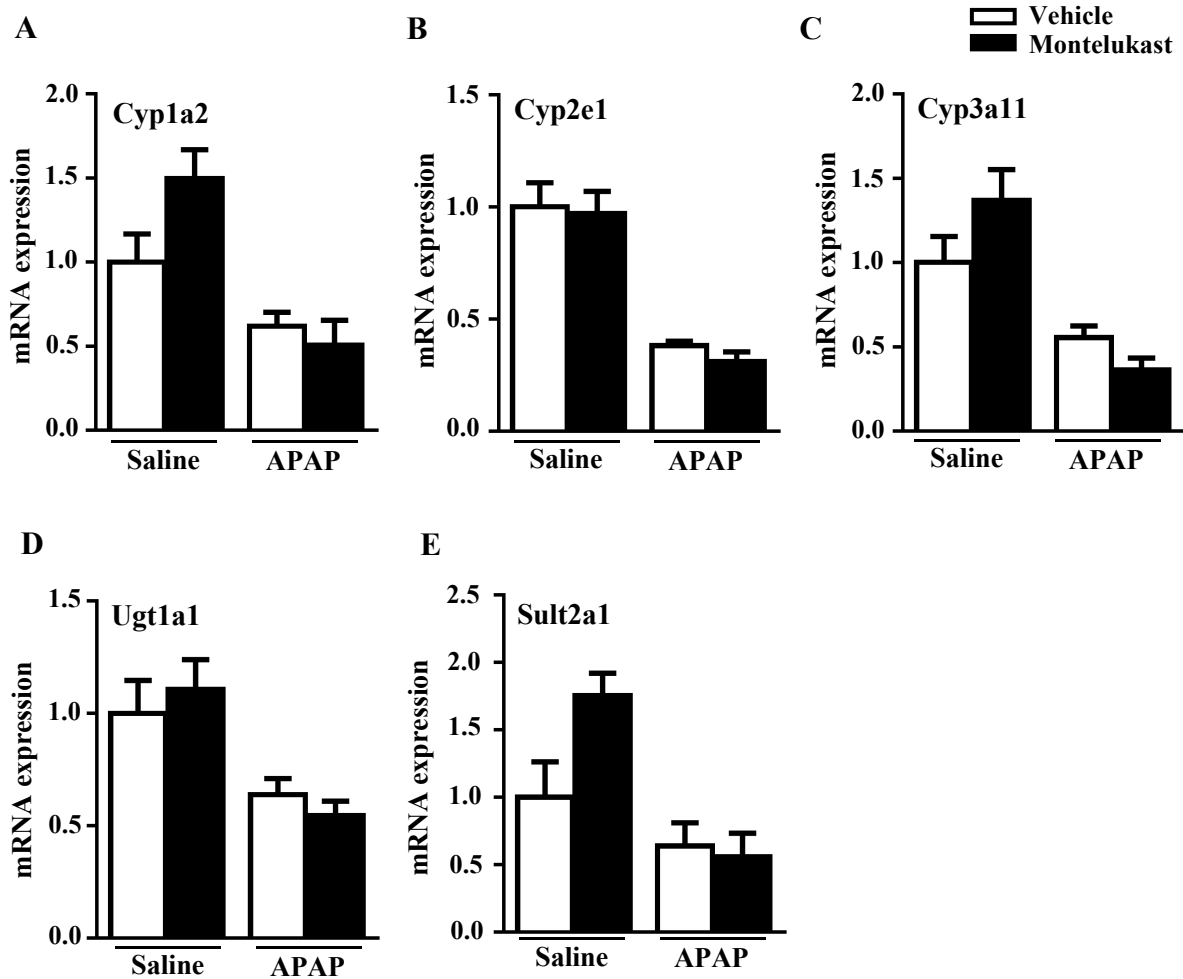
Supplementary Figure 1



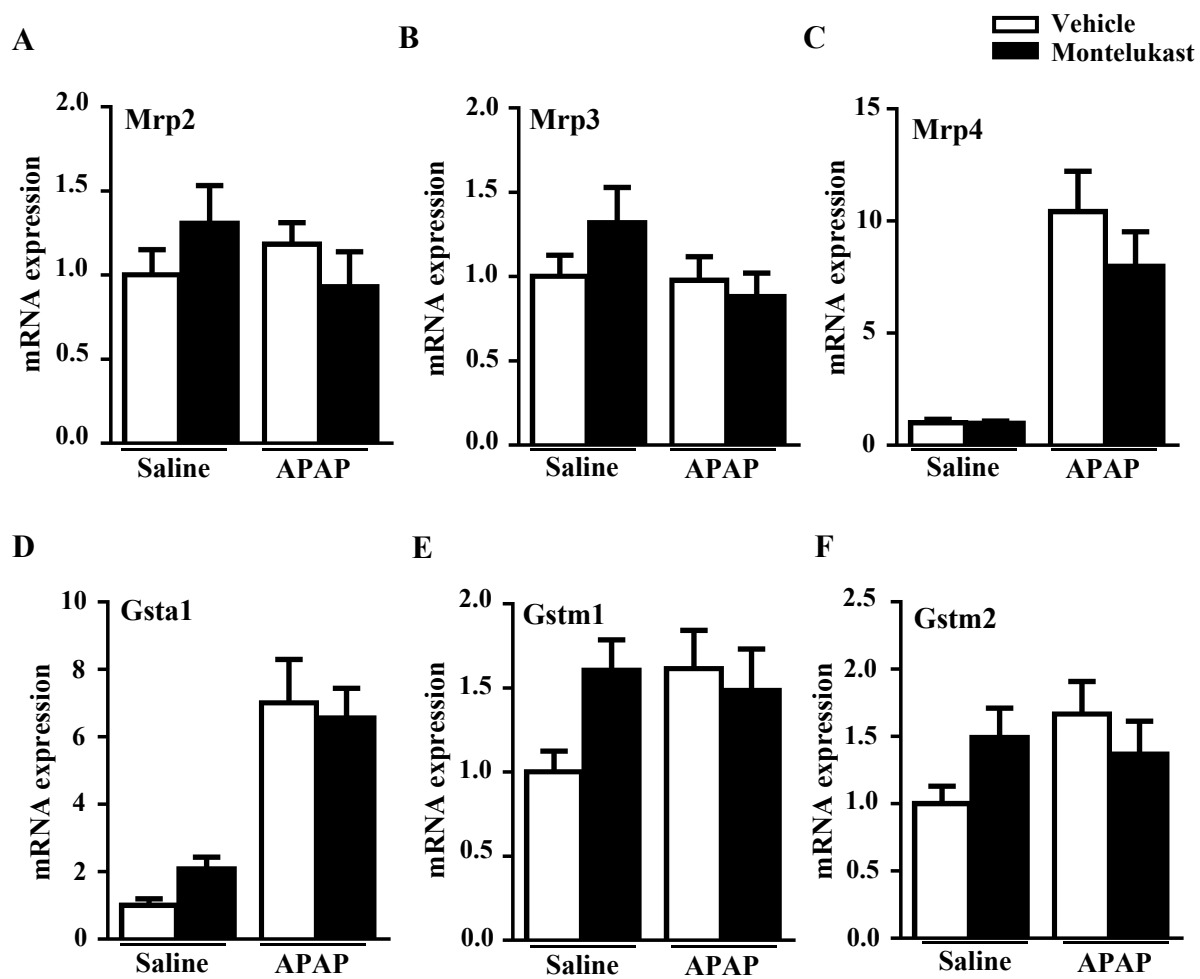
Supplementary Figure 2



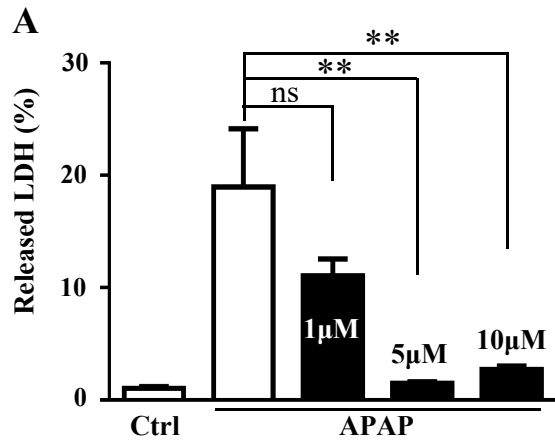
Supplementary Figure 3



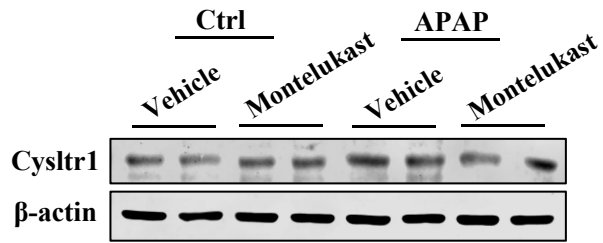
Supplementary Figure 4



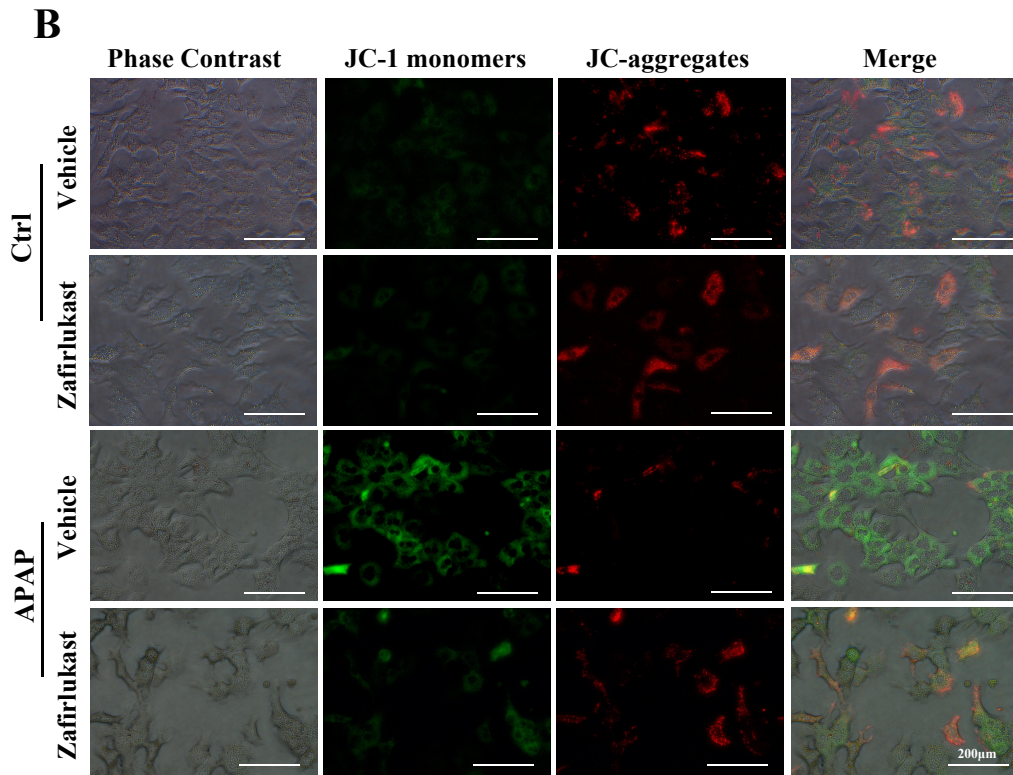
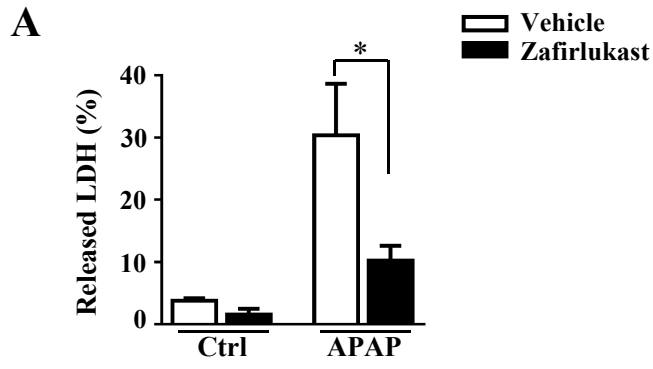
Supplementary Figure 5



B

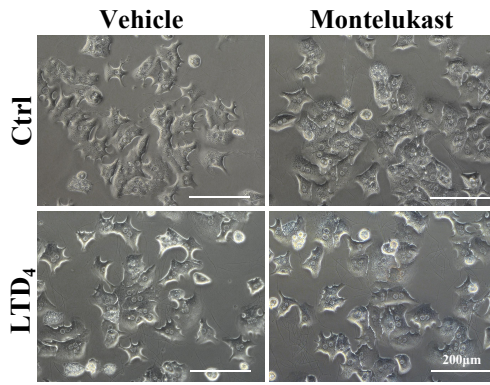


Supplementary Figure 6

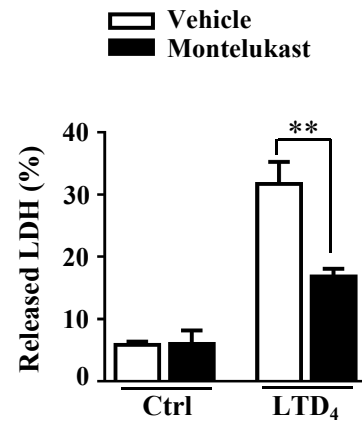


Supplementary Figure 7

A



B



C

