Burke et al. Supporting Information Figure Legends:

Figure 1S: **Effect of MPT inhibitors on APAP-induced $DCFH_2$ oxidation in freshly isolated hepatocytes.** Hepatocytes were incubated with APAP (1 mM). Subsequently, hepatocytes were washed to remove APAP (arrow) and incubated in media alone (triangle), media containing cyclosporine A (10 uM)(CSP) (square), or media containing trifluoperazine (10 uM)(TFP) (diamond) for 2-5h. Control hepatocytes were incubated with media alone for 2h, washed, and subsequently incubated with media alone for 2-5h (circle). In Figure 3, appropriate time points were taken and relative toxicity was measured using ALT release. In this figure hepatocytes were resuspended with 2', 7'-dichlorodihydrofluorescein diacetate (10 μM) for 25 min and fluorescence determined as previously described (*13*). Samples which significantly increased from the 2h wash are indicated by * ($p \leq 0.05$). Samples (n = 3 from separate mice) which are significantly decreased from APAP alone at the same time point are designated by †† (* ($p \leq 0.05$).

Figure 2S: **Effect of NOS inhibitors on APAP -induced $DCFH_2$ oxidation in freshly isolated hepatocytes.** Hepatocytes were incubated with APAP (1 mM) for 2h, washed to remove APAP (arrow), and subsequently incubated in media alone (2-5h) (triangle). Control hepatocytes were incubated in media alone for 2h, washed, and subsequently incubated in media alone (2-5h)(circle). Following washing to remove APAP some hepatocytes shown in A and Figure 4A were incubated with the general NOS inhibitor L-NMMA (1 mM) (diamond) or the nNOS inhibitor 7-nitroindazole (10 μM) (square) (2-5h). Following washing to remove APAP other hepatocytes shown in B and Figure 4B were incubated with the iNOS inhibitors L-NIL (1 mM) (square) or SAIT (1 mM)

(diamond) (2-5h). In Figures 4A and 4B aliquots were taken and toxicity determined by ALT release. Other hepatocytes (A and B) cells were resuspended with 2', 7'-dichlorodihydrofluorescein diacetate (10 μM) for 25 min and fluorescence determined as previously described (*13*). Samples (n = 3 from separate mice) which significantly increased from the same 2 h incubation are indicated by * ($p \leq 0.05$).

Figure 3S: **Effect of reactive nitrogen species scavengers on APAP-induced $DCFH_2$ oxidation in freshly isolated hepatocytes.** Hepatocytes were incubated with APAP (1 mM) for 2 h, washed to remove APAP (arrow), and subsequently incubated in media alone (2-5h) (triangle). Control hepatocytes were incubated in media alone for 2h, washed, and subsequently incubated in media alone (2-5h)(circle). Following washing to remove APAP some hepatocytes were incubated with the RNS scavengers N-acetylcysteine (1 mM) (square) or acetaminophen (50 mM) (diamond)(2-5h). Aliquots from hepatocyte incubations (A) were taken and toxicity determined by ALT release. Other hepatocytes (B) were resuspended with 2', 7'-dichlorodihydro-fluorescein diacetate (10 μM) for 25 min and fluorescence determined as peviously described (*13*). Samples (n = 3 from separate mice) which significantly increased from the same 2h incubation are indicated by * ($p \leq 0.05$).

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Figure 1S

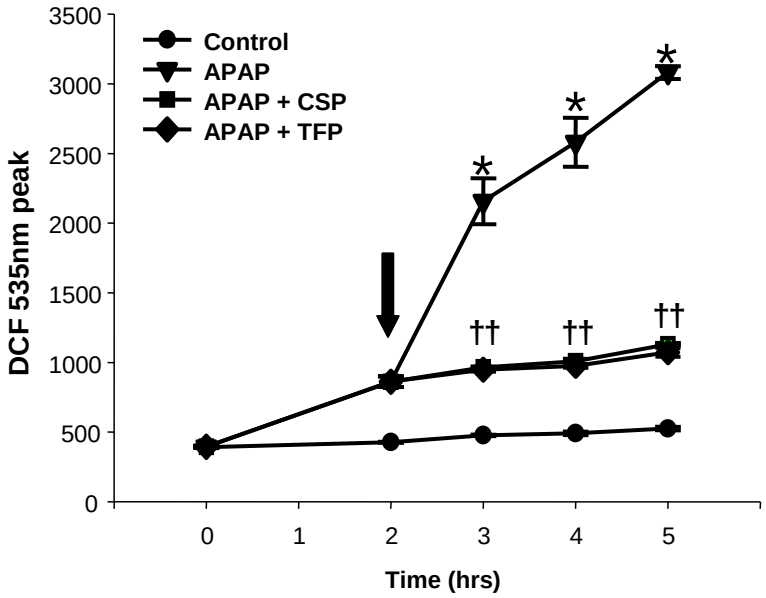


Figure 2SA

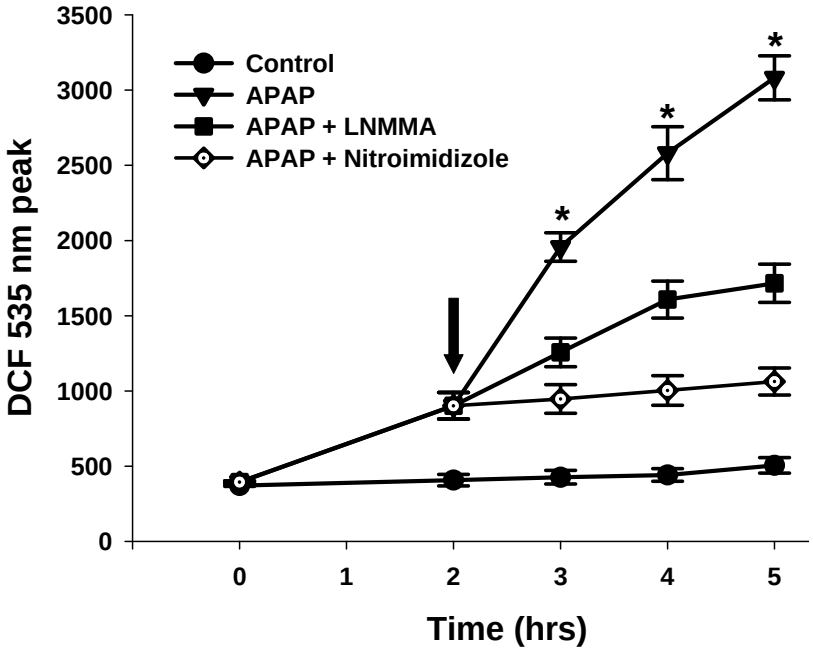

Control
APAP
APAP + LNMMA
APAP + Nitroimidizole
DCF 535 nm peak
Time (hrs)
0
500
1000
1500
2000
2500
3000
3500
0
1
2
3
4
5
*
*
*

Figure 2SB

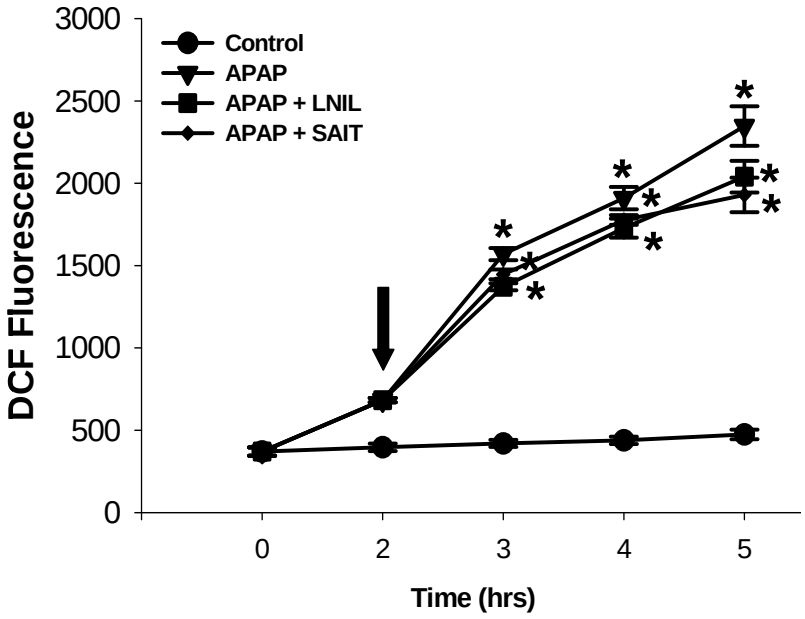
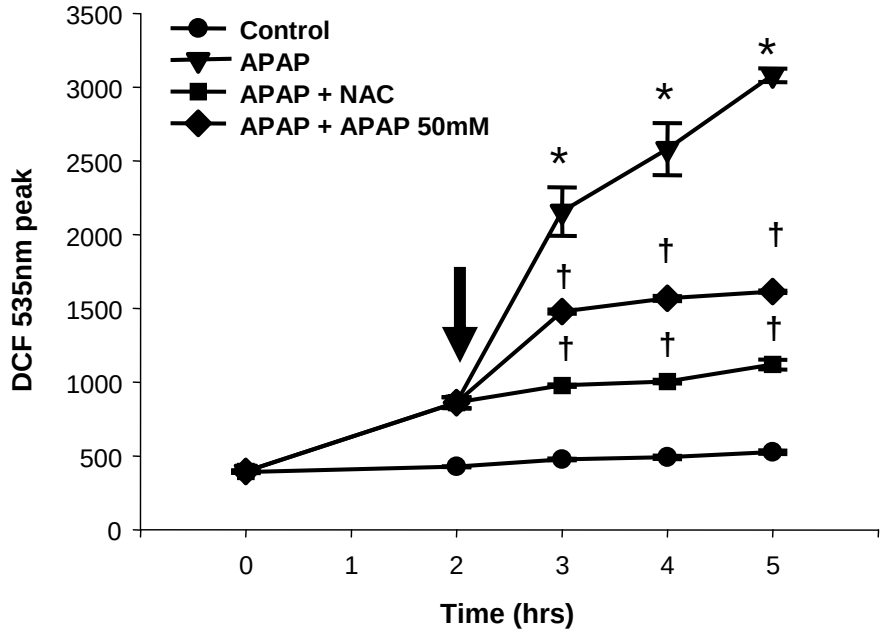

Control
APAP
APAP + LNIL
APAP + SAIT
DCF Fluorescence
3000
2500
2000
1500
1000
500
0
0
2
3
4
5
Time (hrs)

Figure 3


Control
APAP
APAP + NAC
APAP + APAP 50mM
DCF 535nm peak
Time (hrs)
0
500
1000
1500
2000
2500
3000
3500
0
1
2
3
4
5
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