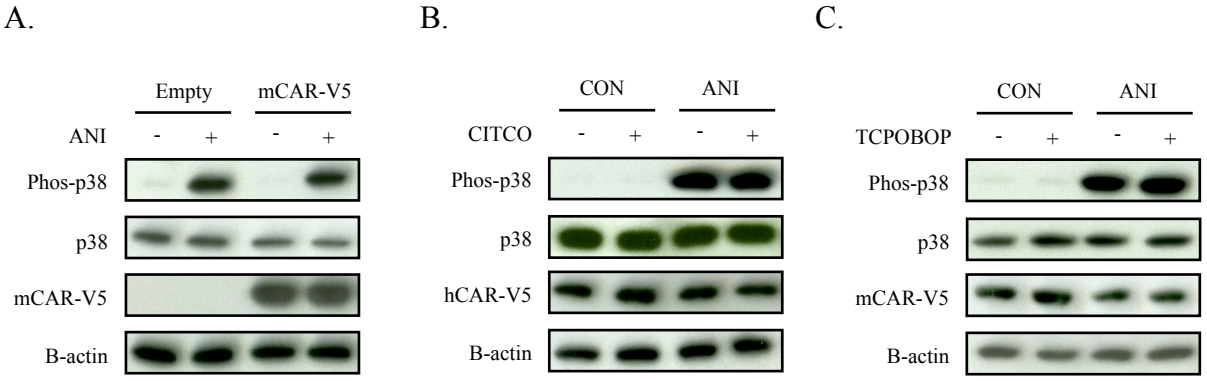
p38 mitogen activated protein kinase regulates the nuclear receptor CAR to activate the *CYP2B6* gene

Kosuke Saito, Rick Moore, and Masahiko Negishi

Drug Metabolism and Disposition



Supplemental Figure 1. Activation of p38 MAPK by anisomycin in HepG2 transiently expressing mouse CAR (A), Yh18 (B) and Ym17 cells (C).
A-C. Cell extracts were prepared as described in Materials & Methods from HepG2 transiently expressing mouse CAR (A), Yh18 (B) and Ym17 cells (C) at 2 hr of anisomycin with CITCO/ TCPOBOP treatment. Protein levels of phosphorylated p38 MAPK (Phos-p38), p38 MAPK (p38) and V5-tagged mouse and human CAR (mCAR-V5 and hCAR-V5, respectively). Protein levels of B-actin were determined as internal control. Data shown are representative of results from two to three individual experiments.

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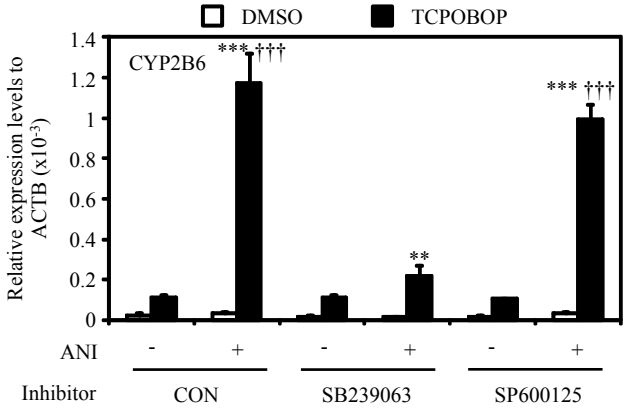

Supplemental Figure 2. Effect of p38 MAPK inhibitor SB239063 on the anisomycin potentiated CYP2B6 induction by CAR in Ym17 cells.
Total RNAs were prepared as described in Materials & Methods from Ym17 cells treated as described Materials and Methods. SB239063 and a JNK inhibitor SP600125 were pre-treated 1 hr before anisomycin and/or TCPOBOP treatment. Expression level of CYP2B6 mRNA was determined. Values are expressed as the relative expression levels normalized to the expression levels of B-actin (ACTB) mRNA. Data are mean ± S.D. (n = 3 or 4 in each group). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$ for comparison between with and without TCPOBOP exposure, ††† $p < 0.005$ for comparison between with and without anisomycin exposure. Newman-Keuls multiple comparison test. CON, control; ANI, anisomycin.