**Activation of the constitutive androstane receptor increases the therapeutic index of CHOP in lymphoma treatment**

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**Supplementary Table S1**: Quantitative proportion of cyclophosphamide (CPA), doxorubicin (DOX), vincristine (VCN) and prednisone (Pred) in the CHOP Regimen.



**Supplementary Fig. S1:** Activation of CAR improves the anticancer activity of the FC (fludarabine, cyclophosphamide) regimen in HPH/HL-60 co-culture. Co-cultured HPH and HL-60 leukemia cells were treated with CPA or FC at indicated concentrations in the presence of CITCO (1 µM) or vehicle control (0.1% DMSO). Viability of HL-60 cells under these treatments was determined at 0, 24, 36, and 48 h. Concentration-(A) and time-dependent (B) anticancer activity of CPA and FC chemotherapy in the presence and absence of CITCO were analyzed. Data represent the mean ± S.D. of three independent measurements normalized as percent viability of vehicle control. Statistical significance between the treatment groups 0.1% DMSO/FC and CITCO/FC were analyzed (\*, *p* < 0.05).

**Supplementary Fig. S2:** CHOP- and DOX-induced cytotoxicity in H9c2 cells. H9c2 cells seeded in 96 well plates were treated with vehicle control (0.1% DMSO) or various concentrations of CHOP (A) and DOX (B) for 24 hours. Cytotoxicity of H9c2 cells were analyzed using MTT assay following the manufacturer’s instructions.

**Supplementary Fig. S3:** Effects of CAR activation on the expression of genes responsible for CHOP disposition in H9c2 cells and rat liver. The expression of Cyp2b2, Cyp3a1, Cyp3a23/3a1, Cbr1, Cbr3, and Abcb1a was measured using total RNA extracted from H9c2 cells following treatment with vehicle control (0.1% DMSO), CITCO (1 μM), TCPOBOP (250 nM), or phenobarbital (1 mM)\*. Expression of these genes was analyzed with RT-PCR. Data represent the mean ± S.D. of three independent experiments.

\*: TCPOBOP and phenobarbital are known rodent CAR activators.