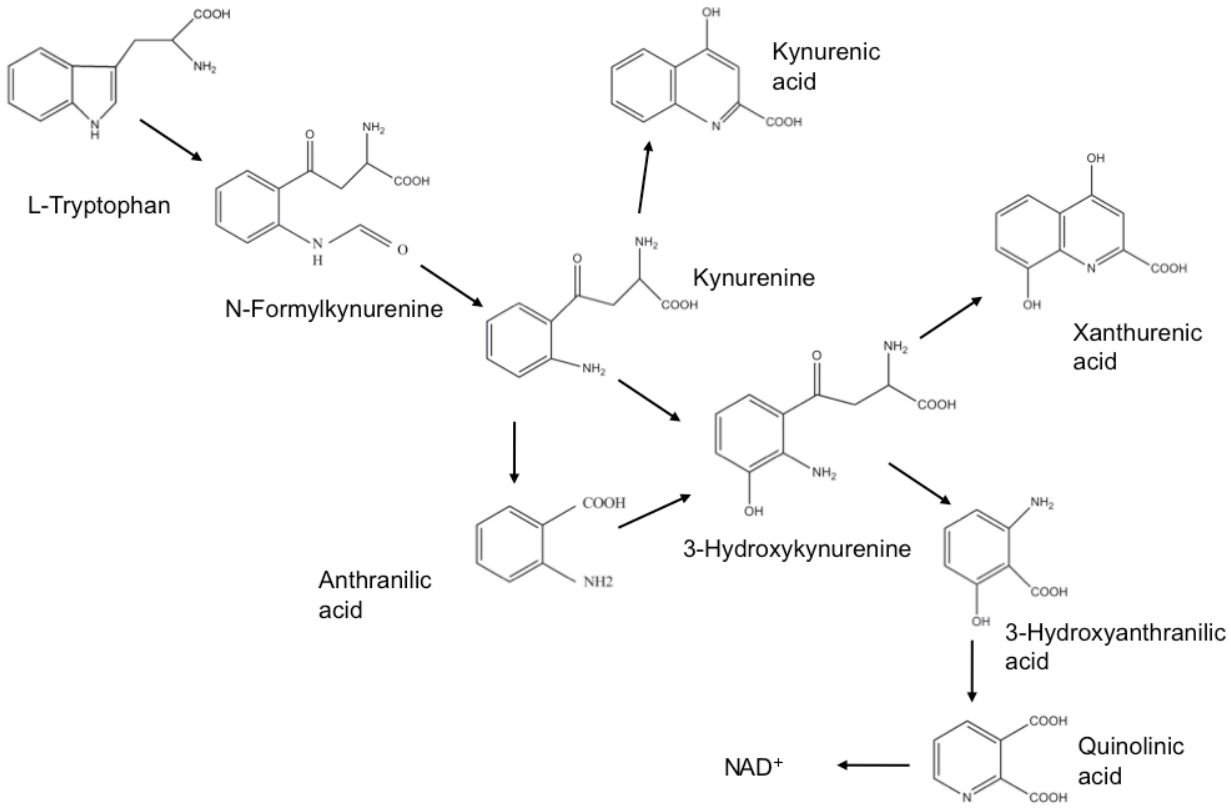
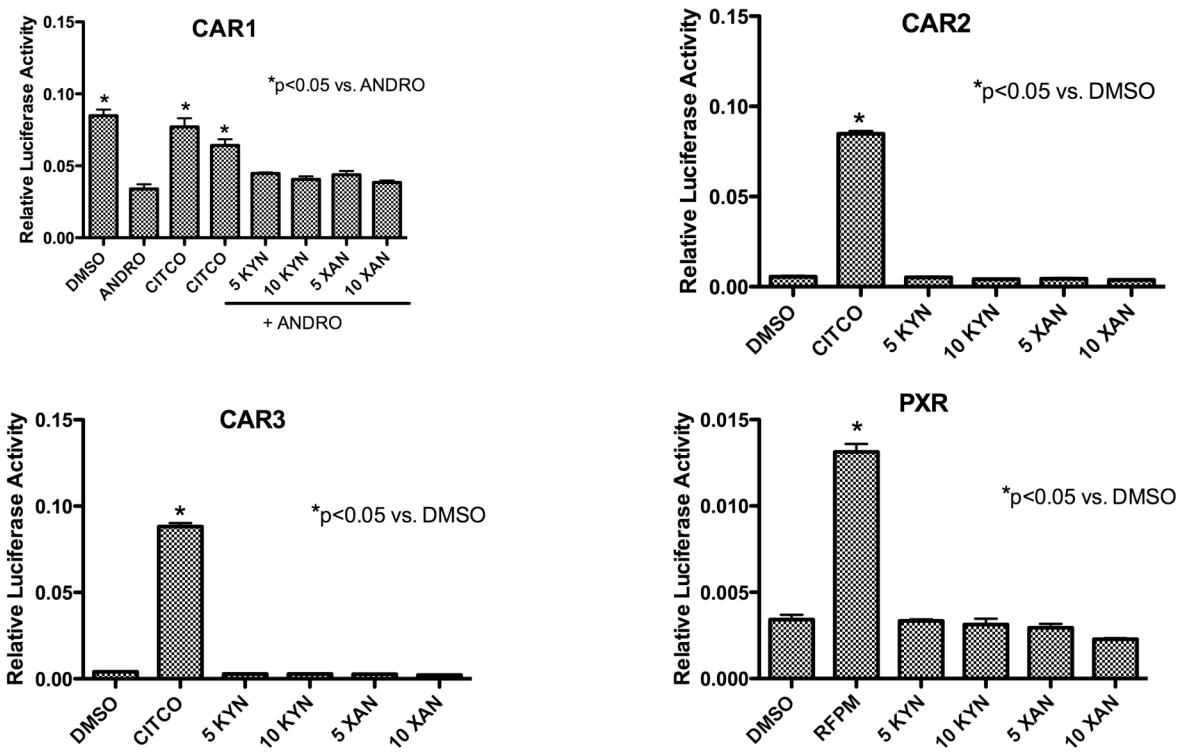


Supplementary Figure 1S. Simplified diagram of the kynurenine pathway of L-tryptophan degradation in mammals depicting the metabolites tested for Ah receptor ligand-mediated activity.



Supplementary Figure 2S. Effect of kynurenic or xanthurenic acid on nuclear receptor activation. COS-1 cells were transfected with 25 ng of CMV2-CAR 1, 2 or 3 or CMV2-PXR expression plasmid, 25 ng 3.1-RXRα expression plasmid, 100 ng of luciferase reporter, and 10 ng of pRL-CMV. After 18 h, cells were treated as indicated and each treatment was performed in quadruplicate. Kynurenic (KYN) or xanthurenic acid (XAN) was added at either 5 or 10 μM., other ligands were added as outlined in supplementary methods section. At 24 h post-treatment, the cells were lysed and analyzed for luciferase activity. All values represent the mean ± standard deviation. The constitutive activity of CAR1 is suppressed by the presence of ANDRO, and this activity can be restored by the CAR ligand CITCO. Neither KAN nor XAN restored CAR1 activity in the presence of ANDRO. In addition, for CAR2, CAR3 and PXR, KYN and XAN had no effect on receptor activation. Thus, KAN and XAN are not activators of CAR or PXR receptors.