# INHIBITION OF NUCLEAR FACTOR (NF)-κB ACTIVITY BY FARNESOID RECEPTOR

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The farnesoid X receptor (FXR; NR1H4)/bile acid receptor belongs to the steroid-like super-family of nuclear receptors. FXR is expressed in the vasculature (Bishop-Bailey *et al*., 2004) and FXR ligands inhibit the induction of iNOS expression by IL-1β in vascular smooth muscle cells (Li *et al*., 2005), a process requiring NF-κB activation (Taylor *et al*., 1998). We have therefore tested whether FXR regulates IL-1β-induced NF-κB activity.

HEK293 cell culture, transfections and luciferase reporter gene assays were as previously described (Bishop-Bailey *et al*., 2000). pNF-κB.Luc (BD Biosciences Clontech) or FXR-responsive reporter gene (IR-1.luc) were co-transfected with combinations of pcDNA-rFXR and/or pcDNA-r-dominant-negative-(DN)-FXR (gifts from Dr. Tom Kocarek, Wayne State University), and control pcDNA3.1 (Invitrogen). 16h post-transfection, cells were treated with IL-1β (10ng/ml; 24h). In some experiments, cells were treated with the FXR ligand, 6α-ethyl-chenodeoxycholic acid (6ECDCA; 30μM) 1h prior to IL-1β addition.

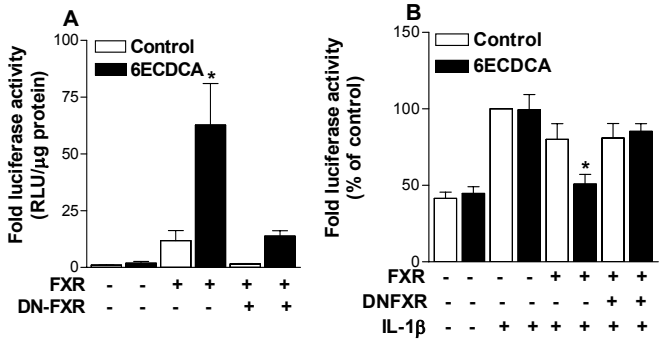


*Figure 1: (A) 6ECDCA activates an FXR-responsive reporter gene and (B) reduces IL-1β-induced NF-κB reporter gene activation in the presence (+), but not the absence (-) of FXR. DN-FXR blocks the effects of 6ECDCA. All data represents mean ± S.E.M. n=9 from 3 experiments. * indicates p<0.05 by one-way ANOVA (Bonferroni's post-test).*

In the presence, but not the absence of transfected FXR, 6ECDCA significantly induced IR-1, an FXR-responsive reporter gene, activity (Figure 1A), and reduced IL-1β-induced NF-κB reporter gene activation (Figure 1B). 6ECDCA-induced FXR activation and NF-κB inhibition were abolished in cells co-transfected with DN-FXR.

FXR activation inhibits IL-1β-induced NF-κB reporter gene activity. FXR may therefore be a novel regulator of vascular inflammation.

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