DMD Manuscript # 90068

Supplemental Data
Drug Metabolism and Disposition

Differential role of LXRα and LXRβ in the regulation of UDP-glucuronosyltransferase 1A1 in humanized UGT1 mice

Hansmann E, Mennillo E, Yoda E, Verreault M, Barbier O, Chen S, Tukey RH

1Laboratory of Environmental Toxicology, Department of Pharmacology, University of California, San Diego, La Jolla, CA 92030-0722, USA.
Figure 1.

(A) In silico analysis of the 10kb promoter sequence of the human UGT1A1 gene (Genebank number AF297093) revealed the presence of 5 degenerated DR4 motifs localized at positions -9903 (a), -9855 (b), -7632 (c), -4076 (d) and -888 (e) bp of the promoter. These elements were assayed for LXRα/RXRα interaction in EMSA by using end-labeled DNA probes, in the presence of in vitro produced RXRα, LXRα or both RXRα and LXRα proteins as indicated. n.s.: non-specific binding.

(B) HK293 cells were transfected with 100ng of empty firefly luciferase (Luc) reporter construct (TKpGL3) or containing 3 copies of the 4 LXRα-interacting DNA motifs identified in A, in the presence of the expression plasmids for LXRα and RXRα (10ng) and the renilla luciferase (pRL-NULL) expression plasmid (30ng). Cells were subsequently treated with ethanol (vehicle) or T0901317 (1µM) for 24H. Values are
expressed as fold induction over the control (vehicle-treated cells) set at 1, normalized to internal renilla activity. Values represent the means ± SD.