Supplementary Table Ia
Constructs used for transactivation assays and maximal activators of the PXRs and VDRs

Receptor	**Expression vector**	**Amount transfected per well (ng reporter vector / ng expression construct)**	**Maximal activator (EC_{50}, μM)**	**Maximal Fold Induction and Concentration Used**
Human PXR	Full-length	25 / 2.7	Rifampicin (0.11 ± 0.013)	4.3 (10 μM)
Human PXR ('SXR')	GAL4/LBD chimera	125/83.3	Rifampicin (0.52 ± 0.007)	11.6 (20 μM)
Human VDR	Full-length	30/3.5	1,25-$(OH)_2$-vitamin D_3 (0.0019 ± 0.00013)	95.0 (1 μM)
Mouse VDR	Full-length	45/4.5	1,25-$(OH)_2$-vitamin D_3 (0.00062 ± 0.00002)	91.8 (0.01 μM)
Mouse PXR	Full-length	25 / 2.7	Pregnenolone 16α-carbonitrile (0.39 ± 0.09)	2.5 (20 μM)
Rat PXR	Full-length	25 / 2.7	Pregnenolone 16α-carbonitrile (0.63 ± 0.13)	6.2 (20 μM)
Rabbit PXR	Full-length	25 / 2.7	5β-Pregnane-3,20-dione (11.8 ± 2.4)	15.5 (50 μM)
Chicken PXR (=CXR)	Full-length	10/1	Nifedipine (0.73 ± 0.31)	2.7 (20 μM)
Frog PXR (=BXRα) (*Xenopus laevis*)	GAL4/LBD chimera	75/50	*n*-Butyl-*p*-amino-benzoate (6.5 ± 1.1)	30.8 (30 μM)
Frog PXR (=BXRβ) (*Xenopus laevis*)	GAL4/LBD chimera	75/50	*n*-Propyl-*p*-hydroxy-benzoate (10.3 ± 1.3)	13.2 (50 μM)
Zebrafish PXR	GAL4/LBD chimera	75/50	5α-Androstan-3α-ol (4.6 ± 0.1)	17.6 (20 μM)
Sea lamprey VDR	Full-length	150/15 (no RXR); 150/15 + 15 ng zebrafish RXRβ/well	1,25-$(OH)_2$-vitamin D_3 (0.036± 0.01 without RXR; 0.024 ± 0.002 with RXR)	23.9 without RXR; 137 with RXR (0.3 μM)

Supplementary Table Ib
Effects of bile salts, bile salt precursors, and benzoates on sea lamprey VDR

Type of Bile Compound	**Species Which Produce the Bile Compound**	**Common name**	**Lamprey VDR `EC_{50} (μM)**	**Lamprey VDR ε**
Bile salt precursor	All species	7α-Hydroxycholesterol	No effect	
C_{24} Bile alcohol, tetra-hydroxylated	**Sea lamprey (*Petromyzon marinus*)**	**5α-Petromyzonol[a]** **Petromyzonol 24-sulfate** **3-Ketopetromyzonol** **3-Ketopetromyzonol sulfate** **3-Keto-7α,12α-dihydroxy-5α-cholanic acid[b]** **5β-Petromyzonol[b]**	**No effect** **~ 1** **No effect** **~ 1** **No effect** **No effect**	 **< 0.06** **< 0.05**
C_{27} bile alcohol, tri-hydroxylated	Bile acid or bile alcohol precursor in many species	5β-Cholestan-3α,7α,12α-triol	No effect	
C_{27} Bile alcohol, tetra-hydroxylated	Hagfish (*Myxine glutinosa*)	5α-Myxinol[c] 5α-Myxinol 3β, 27-disulfate	No effect No effect	
C_{27} Bile alcohol, penta-hydroxylated	Cypriniform fish (zebrafish, goldfish, carp)	5α-Cyprinol[d] 5α-Cyprinol 27-sulfate	No effect ~ 20	 < 0.06
C_{27} Bile alcohol, hexa-hydroxylated	Cartilaginous fish	5β-Scymnol[e] 5β-Scymnol 27-sulfate	No effect No effect	
C_{27} Bile acid	Alligator	3α,7α,12α–Trihydroxy-5β-Cholestan-27-oic acid, taurine conjugated	No effect	
C_{24} Bile acid, primary	Chicken Human	Chenodeoxycholic acid Glycochenodeoxycholic acid Taurochenodeoxycholic acid	No effect No effect No effect	
C_{24} Bile acid, primary	Rat	α-Muricholic acid	No effect	
C_{24} Bile acid, primary	Mouse	β-Muricholic acid β-Muricholic acid - taurine conjugated ω-Muricholic acid	No effect No effect No effect	
C_{24} Bile acid, secondary	Mouse Rat	Murideoxycholic (murocholic) acid	No effect	
C_{24} Bile acid, secondary	Rabbit Human	Deoxycholic acid Glycodeoxycholic acid Taurodeoxycholic acid 7-Ketodeoxycholic acid	No effect No effect No effect No effect	
C_{24} Bile acid,	Human	Cholic acid	No effect	

primary		Glycocholic acid Taurocholic acid Allocholic acid[f]	No effect No effect No effect	
C_{24} Bile acid, primary	Various mammals	Hyodeoxycholic acid Taurohyodeoxycholic acid	No effect No effect	
C_{24} Bile acid, secondary and metabolites thereof	Human	Lithocholic acid Glycolithocholic acid Taurolithocholic acid 7-Ketolithocholic acid 12-Ketolithocholic acid 7,12-Diketolithocholic acid Lithocholic acid 3-sulfate Glycolithocholic acid 3-sulfate Taurolithocholic acid 3-sulfate 3-Ketolithocholic acid Lithocholic acid acetate Lithocholic acid acetate methyl ester	No effect No effect No effect No effect No effect No effect No effect No effect No effect No effect No effect No effect	
Short-chain bile acids		23-Nordeoxycholic acid 23-Norcholic acid	No effect No effect	
Benzoates		3-Aminoethylbenzoate *n*-Butyl-*p*-aminobenzoate *n*-Propyl-*p*-hydroxybenzoate	No effect No effect No effect	

[a] 5α-Cholan-3α,7α,12α,24-tetrol
[b] 3-Keto-7α,12α-dihydroxy-5α-cholanic acid is the bile acid derivative of 3-ketopetromyzonol. 5β-Petromyzonol is studied for comparison to 5α-petromyzonol.
[c] 5α-Cholestan-3β,7α,16α,27-tetrol
[d] 5α-Cholestan-3α,7α,12α,26,27-pentol
[e] 5β-Cholestan-3α,7α,12α,24, 26,27-hexol
[f] Allocholic acid is 5α-cholic acid and is studied for comparison to (5β-)cholic acid.

Supplementary Table Ic

Effects of bile salts and bile salt precursors on frog BXRs

Common name	Importance	BXRα EC_{50} (μM)	BXRα PXR ε	BXRβ EC_{50} (μM)	BXRβ PXR ε
7α-Hydroxycholesterol	Bile salt precursor	No effect		No effect	
5β-Cholestan-3α,7α,12α-triol	Bile acid and alcohol precursor	No effect		No effect	
5β-Myxinol 5β-Myxinol-3β,27-disulfate	Bile alcohol (hagfish)	No effect No effect		No effect No effect	
5α-Cyprinol **5α-Cyprinol sulfate[a]**	**Bile alcohol (fish and frogs)**	**No effect** **No effect**		**No effect** **No effect**	
5β-Scymnol 5β-Scymnol sulfate	Bile alcohol (cartilaginous fish)	No effect No effect		No effect No effect	
3α,7α,12α̃-Trihydroxy-5β-Cholestan-27-oic acid, taurine conjugated[a]	**Long-chain bile acid from alligator (similar to frog bile acids)**	**No effect**		**No effect**	
Deoxycholic acid	Major biliary surfactant for rabbits	No effect		No effect	
Chenodeoxycholic acid	Major primary bile acid in birds and mammals	No effect		No effect	
Cholic acid	Major primary bile acid in birds and mammals	No effect		No effect	
Lithocholic acid	Toxic secondary bile acid in birds and mammals	No effect		No effect	
Murideoxycholic acid	Secondary bile	No effect		No effect	

	acid in mice and rats				
n-Butyl-*p*-aminobenzoate		6.5 ± 1.1	1.0[b]		
n-Propyl-*p*-hydroxybenzoate				10.3 ± 1.3	1.0 [b]

[a] *Xenopus laevis* bile contains a mixture of bile alcohol sulfates and C_{27} bile acids similar to these two compounds.
[b] Reference 'maximal activator' with $\varepsilon = 1.0$.