

Supplemental figure 1

A.

DNA-binding domain

LXRa_human	ELCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKG--AHYICHSGGHCPMDTYMRRKCQEC
LXRa_mouse	ELCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKG--ARYVCHSGGHCPMDTYMRRKCQEC
LXRa_platypus	ELCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKG--ARYTCHSGGHCPMDTYMRRKCQEC
LXRa_chicken	EVCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKG--AQYVCKNGGKCEMDMYMRRKCQEC
LXRa_xen_laevis	EVCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKN--AQYSCKNNGKCQMDMYMRRKCQEC
LXRa_xenopus_trop	EVCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKN--AQYTCKNNGKCQMDMYMRRKCQEC
LXRa_zebrafish	EVCSVCGDKASGFHYNVLSCE EGCKG FFRRSVIKG--AQYSCKNSGRCEMDMYMRRKCQEC
LXR_ciona	EVCLICGDKASGYHYGVLSCE EGCKG FFRRCI IKT--PNFKCKNNGQCQMDTYMRRKCQKC
LXR_sea_urchin	ELCLVCGDRASGFHYNALSCE EGCKG FFRRSITKN--AKYNCTRGGNCEMDMYMRRKCQEC
LXRb_human	ELCRVCGDKASGFHYNVLSCE EGCKG FFRRSVVVGARRYACRGGGTCQMDAFMRRKCQEC
LXRb_mouse	ELCRVCGDKASGFHYNVLSCE EGCKG FFRRSVVHGGAGRYACRGSSTCQMDAFMRRKCQEC

LXRa_human	RLRKCQRQAGM
LXRa_mouse	RLRKCQRQAGM
LXRa_platypus	RLRKCQRQAGM
LXRa_chicken	RLRKCQEAGM
LXRa_xen_laevis	RLRKCREAGM
LXRa_xenopus_trop	RLRKCREAGM
LXRa_zebrafish	RLRKCREAGM
LXR_ciona	RLDKCRAAGM
LXR_sea_urchin	RLRKCREVGM
LXRb_human	RLRKCKEAGM
LXRb_mouse	RLRKCKEAGM

B.

Ligand-binding domain

		<u>Helix-1</u>		<u>Helix-3</u>
LXRa_human	206	--LSPEQLGMIEKLVAAQQQCNRRSFS	SDRLRVTPWPMAPDPHSREARQQR	FAHFTE LAI
LXRa_mouse		--LSPEQLGMIEKLVAAQQQCNRRSFS	SDRLRVTPWPIAPDPQSREARQQR	FAHFTE LAI
LXRa_platypus		--LSPEQLGMIEKLVAAQQQLCNRRSFS	DQLRVTPWPMAPDPQSREARQQR	FAHFTE LAI
LXRa_chicken		--LTPEQLNMIKLVAAQQQCNQRSFT	DRLKVTWPWPQVPDPNNREARQQR	FAHFTE LAI
LXRa_xen_laevis		--LTPQQEKMIQLVSAQQQCNKRSFS	DQPKVTPWPPGTDPNREARQQR	FAHFTE LAI
LXRa_xenopus_trop		--LTPQQEKMIQQLVSAQQQCNKRSFS	DQPKVTPWPLGSDPNREARQQR	FAHFTE LAI
LXRa_zebrafish		--LAPEQQEMIEKLVAMQKQCNKRSF	IDRPKVTWPWQSDPQNRVQR	FAHFTE LAI
LXR_ciona		--LTSHQRNLVEMLQANEARFQWPT	QEAQVTPWVESGDS-HRCRAS-	FAHFTE LAI
LXR_sea_urchin		--LTDEQREVIENLVSIHKELEIP	GPEDLKRVTWPWKEGQNS-----	FAHITEL TI
LXRb_human	218	VQLTAAQELMIQQLVAAQLQCNKRS	SFSQPKVTPWPLGADPQSRDARQQR	FAHFTE LAI
LXRb_mouse		IQLTAAQELMIQQLVAAQLQCNKRS	SFSQPKVTPWPLGADPQSRDARQQR	FAHFTE LAI

		<u>Helix-3</u>	<u>Helix-4</u>	<u>Helix-5</u>
LXRa_human	263	VSVQEIVDFAKQLPGFLQLSREDQI	ALLKTS	SAIEV M LLETSRRYNPGSESITFLKDFSY
LXRa_mouse		VSVQEIVDFAKQLPGFLQLSREDQI	ALLKTS	SAIEV M LLETSRRYNPGSESITFLKDFSY
LXRa_platypus		VSVQEIVDFAKQLPGFLQLSREDQI	ALLKTS	SAIEV M LLETSRRYNPGSESITFLKDFSY
LXRa_chicken		ISVQEIVDFAKQLPGFRELTR	EDQI	ALLKTS
LXRa_xen_laevis		ISVQEIVDFAKQVPGFLELSREDQI	ALLKAS	TIEIMLLETARRYNHETECITFLKDFTY
LXRa_xenopus_trop		ISVQEIVDFAKQIPGFLELSREDQI	ALLKAS	TIEIMLLETARRYNHETECITFLKDFTY
LXRa_zebrafish		MSVQEIVDFAKQLPGFLELTREDQI	ALLKTS	TIEIMLLETARRYNPAIDSITFLKDFTY
LXR_ciona		LIVQLVVEFTKQLPGFLT	VSREDQI	ILLKACTIEVMLLRAAKQYDKKSKAINFLNGKIFY
LXR_sea_urchin		LTIQLIVEYSKHIPGFLT	TLTREDQI	ILLKGS
LXRb_human	277	ISVQEIVDFAKQVPGFLQLGREDQI	ALLKAS	TIEIMLLETARRYNHETECITFLKDFTY

LXRb_mouse		ISVQEIVDFAKQVPGFLQLGREDQIALLKASTIEIMLLETARRYNHETECITFLKDFTY
		<u>Helix-6</u> <u>Helix-7</u> <u>Helix-8</u>
LXRa_human	322	NRED FAKAGLQ VEFINPIFEFSRAMNELQLNDAEFALLIAISIFSADRPNVQDQLQVER
LXRa_mouse		NRED FAKAGLQ VEFINPIFEFSRAMNELQLNDAEFALLIAISIFSADRPNVQDQLQVER
LXRa_platypus		NRDD FAKAGLQ VEFINPIFEFSRSMNELHLNDAEFALLIAISIFSADRPNVQDQPQVEQ
LXRa_chicken		NRDD FAKAGLQ VEFINPIFEFSKGMNELQLNDAEYALLIAINIFSADRPNVQDQSLVER
LXRa_xen_laevis		SKDDFHRAGLQVEFINPIFEFSRGMQMLDDEAYALLIAINIFSADRPNVLNHQHVEN
LXRa_xenopus_trop		SKDDFHRAGLQVEFINPIFEFSRGMQMLDDEAYALLIAINIFSADRPNVQNHQLVEN
LXRa_zebrafish		NKED FAKAGLQ LEFINPIFEFSKGMNDLHLDEAYALLIAINIFSADRPNVQDHELVER
LXR_ciona		DKSSFYRAGMQVEFVDPIDFCNSMAQLGLNEAYALLVAINTFSADRPNIKDMHKVEA
LXR_sea_urchin		TRKQLLEGGIG-DLVDPMYNFAKSMSELDLDYAEFILLMAITILSPDRPAINERERVEQ
LXRb_human	336	SKDD FHRAGLQ VEFINPIFEFSRAMRRLGLDDAEYALLIAINIFSADRPNVQEPGRVEA
LXRb_mouse		SKDDFHRAGLQVEFINPIFEFSRAMRRLGLDDAEYALLIAINIFSADRPNVQEPSRVEA
		<u>Helix-9</u> <u>Helix-10</u> <u>Helix-11</u>
LXRa_human	381	LQHTYVEALHAYVSIHHPHDRLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXRa_mouse		LQHTYVEALHAYVSIHHPHDRLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXRa_platypus		LQHTYVEALHAYVSIHHPQDPLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXRa_chicken		LQHTYVEALHSYICINRPNDHLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXRa_xen_laevis		LQLPYVEALHSYTRIKRPQDHLMFPRLMKLVSLRTLSSVH SEQFF ALRLQDKKLPPLLS
LXRa_xenopus_trop		LQLPYVEALHSYTRIKRPQDHLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXRa_zebrafish		LQQPYVDALHSYIRIKRPNDHLMFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
LXR_ciona		VQNSYVELLRVYLKIHHPDPLMFPRTLMKLVSLRTLNNYH SEQIF ALKVQDKQLPPLLA
LXR_sea_urchin		MQETYLDMLRSYLKLRPHEVLLLPKVLMKLTSLRSLNNSHSELLFQLKVKDQKIPPLLQ
LXRb_human	395	LQQPYVEALLSYTRIKRPQDQLRFPRLMKLVSLRTL SSVHSEQVF ALRLQDKKLPPLLS
LXRb_mouse		LQQPYVEALLSYTRIKRPQDQLRFPRLMKLVSLRTLSSVH SEQVF ALRLQDKKLPPLLS
		<u>Helix-12</u>
LXRa_human	441	EIWDV H E
LXRa_mouse		EIWDV H E
LXRa_platypus		EIWDV H D
LXRa_chicken		EIWDV H E
LXRa_xen_laevis		EIWDV H E
LXRa_xenopus_trop		EIWDV H E
LXRa_zebrafish		EIWDV H E
LXR_ciona		EIWD M
LXR_sea_urchin		EIWD
LXRb_human	455	EIWDV H E
LXRb_mouse		EIWDV H E

Supplemental Figure 1: Sequence alignment DNA-binding and ligand-binding domains of LXRs. **(A)** Sequence alignment of the DNA-binding domain of selected LXRs including the *Ciona intestinalis* and purple sea urchin LXR orthologs. The P-box is highlighted in **bold** type. Nine invariant cysteine residues and the P-box are identical throughout all LXRs, including the putative LXR orthologs in *Ciona intestinalis* and purple sea urchin. **(B)** Sequence alignment of the ligand-binding domains of selected LXRs and their putative invertebrate orthologs. The location of the α -helices above the amino acid sequences are based on the human LXR β crystal structure (Hoerer et al., 2003). Amino acid residues highlighted in **bold** type are residues in human LXR α (Svensson et al., 2003), mouse LXR α (Jaye et al., 2005), and human LXR β (Färnegårdh et al., 2003; Hoerer et al., 2003; Williams et al., 2003) shown to interact with ligands in structures determined by x-ray crystallography. The ligands co-crystallized with the various receptors are: human LXR α – T-0901317 (Svensson et al., 2003); mouse LXR α – GSK3987 (Jaye et al., 2005); and human LXR β – 24(S),25-epoxycholesterol (Williams et al., 2003), T-0901317 (Färnegårdh et al., 2003; Hoerer et al., 2003; Williams et al., 2003), and GW3965 (Färnegårdh et al., 2003).

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