

A. DNA-binding domain

PXR_human	QICRVCGDKATGYHFNVTCEGCKGFFRRAMKRNARLRCPFKRGACEITRKTRRQCQACR
PXR_mouse	QICRVCGDKANGYHFNVTCEGCKGFFRRAMKRNVRLRCPFKRGTCETIRKTRRQCQACR
PXR_rat	QICRVCGDKANGYHFNVTCEGCKGFFRRAMKRNVRLRCPFKRGTCETIRKTRRQCQACR
PXR_rabbit	QTCRVCGDKANGYHFNVTCEGCKGFFRRTVKRNARLRCPFKRGACEITRKTRRQCQACR
PXR_chicken	KVCAVCGDRATGYHFHVMSCGCKGFFRRSILKGVHFTCPF-TRSCPITKAKRRQCQACR
BXR-alpha	KICRACGDRATGYHFNAMTCEGCKGFFRRAMKRNLRRLSCPF-QNSCVINKNNRRHCQACR
BXR-beta	KICRACGDRATGYHFNAMTCEGCKGFFRRAMKRNLRRLSCPF-QNSCVINKNNRRHCQACR
PXR_xentrop	KICRACGDRATGYHFNAMTCEGCKGFFRRAMKRKLQLSCPF-QNSCVINKSNRRHCQACR
PXR_zebrafish	KICQVCGDKSTGYHFNAMTCEGCKGFCRRAMKRPAQLCCPF-QSACVITKSNRRQCQSCR
VDR_PXR_Ciona	-----MHFGAITCEGCKGFFRRSVKKNASFSCAF-EKKCEINKNNRKHCQACR
PXR_human	LRKCLES GM
PXR_mouse	LRKCLES GM
PXR_rat	LRKCLES GM
PXR_rabbit	LRKCLES GM
PXR_chicken	LQKCLDVGM
BXR-alpha	LKKCLDIGM
BXR-beta	LKKCLDIGM
PXR_xentrop	LKKCLDIGM
PXR_zebrafish	LQKCLSIGM
VDR_PXR_Ciona	FNACLAAGM

B. Ligand-binding domain

		<u>Helix-1</u>		
PXR_human	141	QGLTEEQRMIRELMDAQMKTFDTTFSHFKNFRLPGVLSGCELPELQAP-SREEA-AK		
PXR_mouse		QGLTEEQQALIQELMDAQMQTFDTTFSHFKDFRLPAVFHSGCELPEFLQAS-LLEDP-AT		
PXR_rat		QGLTEEQQALIQELMDAQMQTFDTTFSHFKDFRLPAVFHSDCELPEVLQAS-LLEDP-AT		
PXR_rabbit		QGLTGEQRMII EELMDAQMKTFDTTFSHFKNFRLPEVLGSGCEIPELQAL-TEEEA-GR		
PXR_chicken		GGLTAEQQELISILIAAHKRTFDSSFSQFQHYQPAVRLC----IPGPCSQS-PPGPG-V		
BXR-alpha		ASLTPEQQHFLTQLVGAHTKTFDFNFSTFSKNFRPIRRSSDPTQEPQAT-----		
BXR-beta		ASLTPEQQHFITELVEAHTKTFDFNFSTFSKNFRPIRRSPDPTQDPQAT-----		
PXR_xentrop		TSLTPEQQHFVTELAGAHTKTFDFNFSSFKNFRPIKRSSDPTQDPQAT-----*		
PXR_zebrafish		VTLTPQQEAVIQELLNAHKKTFDMTCAHFSQFRPLDRDQKSVSESSPLTNG-SWIDH-RP		
VDR_PXR_Ciona		TRMTMDEKLLVKTLKGRDSYDFAYVEYDTRFGREDGQOEIGNNTENPNG---LDA-AT		
		<u>Helix-3</u>		
PXR_human	199	WSQVRKDLCSLKVSLQL-RGEDGSVWNYKPP-----ADSGGKEIFSLLPHMADMSTYMFK		
PXR_mouse		WSQIMKDRVPMKISLQL-RGEDGSIWNYQPP-----SKSDGKEIIPLLPHLADVSTYMFK		
PXR_rat		WSQIMKDSVPMKISVQL-RGEDGSIWNYQPP-----SKSDGKEIIPLLPHLADVSTYMFK		
PXR_rabbit		WRQIQEELGTMKLSLQL-RGEDGSVWNYTTP-----ADRSGKCLFSLLPHLADMSTYMFK		
PXR_chicken		SASLSPQLDCLDEDVL-----PDVFSILPHFADLSTFMIQ		
BXR-alpha		-----SSEAFMLPHISDLVTYMIK		
BXR-beta		-----SSEAFMLPHISDLFTYMLK		
PXR_xentrop		-----SSGAFMLPHISDLITYMIK		
PXR_zebrafish		IAEDPMQWVFNPTSLSS-SSSSYQSLDNKEK-----KHFKSGN-FSSLPHFTDLTTYMIK		
VDR_PXR_Ciona		AVEAQSTTEDSGKQLHL-MLLFQHFLPIYP-----FSFDPKA-KQLFQHFCDIMTWGIR		
		<u>Helix-3</u>	<u>Helix-4</u>	<u>Helix-5</u>
PXR_human	253	GIISFAKVISYFRDLPIEDQISLLKGAAFELCQLRFNTVFNAET-GTWECGR--LSY---C		
PXR_mouse		GVINFAKVISYFRDLPIEDQISLLKGFATFEMCILRFNTMFDTET-GTWECGR--LAY---C		
PXR_rat		GVINFAKVISHFRELPIEDQISLLKGFATFEMCILRFNTMFDTET-GTWECGR--LAY---C		

PXR_rabbit	GIINFAKVISYFRDLPIEDQISLLKGATLELCLLRFNTVFNAET-GTWECGR--LSY---C
PXR_chicken	QVIKFAKEIPAFRGLPIDDQISLLKGATLGICQIQFNTVFNEET-NAWECGQ--HCF---T
BXR-alpha	GIISFAKMLPYFKSLDIEDQIALLLKGSVAEVS VIRFNTVFNPDT-NTWECGP--FTY---D
BXR-beta	GVISFAKMLPYFRSLAIEDQIALLLKGSVLEVCVIRFNRMFNPKT-NTWECGA--FTY---N
PXR_xentrop	GVISFAKMLPYFKSLNIEDQIALLLKGSVVEVCVIRFNTMFPET-NSWECGP--ITY---N
PXR_zebrafish	NVINFGKTLTMFRALVMEDQISLLKGATFEIILIHFNMFNEVT-GIWECGP--LQY---C
VDR_PXR_Ciona	KVIDYCKGIPQFVQLSIVDQIVLLRGGCLEMLVLRSYFAFSCNE-NKYMSDK--FQY---K

		<u>Helix-7</u>	<u>Helix-8</u>	<u>Helix-9</u>
PXR_human	308	L EDT-AGGF----QQLLLEP M LKFHYMLK K LQLH E EEYVLMQ A ISLFS P DRPGV L QHR V		
PXR_mouse		FEDP-NGGF----QKLLLDPLMKFHC M LK K LQLH K EEYVLMQ A ISLFS P DRPGV V Q R SV V		
PXR_rat		FEDP-NGGF----QKLLLDPLMKFHC M LK K LQLR E EEYVLMQ A ISLFS P DRPGV V Q R SV V		
PXR_rabbit		VEDP-EGGF----QQIYLEPL L KF H ISL K KLRLH E AEYVLLV A MLL F SPD H AS V T Q R D F I		
PXR_chicken		IKDGALAGF----QQIYLEPL L KF H ISL K KLRLH E AEYVLLV A MLL F SPD H AS V T Q R D F I		
BXR-alpha		TEDMFLAGF----RQLFLEPL V RI H RM M R K LN L Q S E E Y A MM A AL S IF A SD R PG V CD W E K I		
BXR-beta		ADDMTMAGF----SQQFLEPL L RI H CM M T K LN L E S E A Y A LM A T M AL F SS D R P GV S D C E K I		
PXR_xentrop		TEDMTMAGF----RQLFLEPL L RM H RM M R K LN L H N E E Y A LM A AM A L F AS D R P GV Q D C CK I		
PXR_zebrafish		MDDAFRAGF----QHLLDP M MM F HY T LR K LR L H E EEYVLMQ A LSLFS P DRPG V T D H K V I		
VDR_PXR_Ciona		PSDFLQAGG----NKEF V E K Y N SL H IR M R K M K LQ V E E IC L LL L AL V LF S PD R PG L E D Q A K V		

		<u>Helix-9</u>	<u>Helix-10</u>
PXR_human	363	DQLQE Q FAITL K SYIE C NR-PQPA H R F FL K IM A ML T EL R SINA Q H T Q R LL R I Q DI H P F A	
PXR_mouse		DQLQ E R F AL T L K AYIE C SR-PYP A H R FL F L K IM A VL T EL R SINA Q Q T Q Q LL R I Q D S H P F A	
PXR_rat		DQLQ E R F AL T L K AYIE C SR-PYP A H R FL F L K IM A VL T EL R SINA Q Q T Q Q LL R I Q D T H P F A	
PXR_rabbit		DQLQ E R F AITL K AYIE C SR-PQ P TH R FL F L K IM A VL T EL R TINA Q H T Q R LL R I Q D T H P F A	
PXR_chicken		DQLQ E K V AL T L K SYID H R H -PM P E G R F L Y AK L LL L L L TEL Q T L K M EN T R Q IL H I Q D L SS M -	
BXR-alpha		Q K LQ E H I AL T L K D F IDS Q R P PS L Q N RL L Y P K I ME C L T EL R T V ND I HS K Q L LE I W D I Q P D A	
BXR-beta		Q N LQ E H I AL M L K AF I ES H R P SP Q N R L L Y P K I ME C L T EL R T I ND I HS K Q L ME I W D I Q P D V	
PXR_xentrop		Q N LQ E H I AL M L K RYIE C Q R PL S Q N RL L Y P K I ME C L T EL R T V ND I HS K Q L LE I W D I Q P D A	
PXR_zebrafish		DR N Q E T L AL T L K TYIE A K R -NG P E K H L L F PK I MG C L E M R S M N E E Y T K Q V L K I Q D M Q P E V	
VDR_PXR_Ciona		E Q M Q D C V A N T L Q A Y E Y TH K -PP N ESS F L Q A R T M Y C L P IL R T I N M L F A Q N I M S L Q T N E K D M	

PXR_human	422	T-PL M Q E LF G IT G S
PXR_mouse		T-PL M Q E LF S ST D G
PXR_rat		T-PL M Q E LF S ST D G
PXR_rabbit		T-PL M RE L F S T T D D
PXR_chicken		T-PL L SE I I S
BXR-alpha		T-PL M RE V F G S P E
BXR-beta		T-PL M RE V F G SL N E
PXR_xentrop		T-PL L RE V F G SH N D
PXR_zebrafish		S-PL W LE I I S K D T
VDR_PXR_Ciona		N-PL I LE V N N S A D E D

Additional file 1: Sequence alignment of (A) DNA-binding domain and (B) ligand-binding domain of PXR from diverse vertebrate species and chordate invertebrate *Ciona intestinalis*. The ligand-binding domain is annotated with the α -helices [1]. Residues highlighted in **bold** are residues shown to contact ligand in crystal structures of human PXR bound to SR121813 [2, 3], hyperforin [4], rifampicin [5], T-0901317 [6], and 17 β -estradiol [7]. Accession numbers are: human PXR [Genbank:AF061056], mouse PXR [Genbank:AF031814], rat PXR [Genbank:AF151377], rabbit PXR [Genbank:AF188476], chicken PXR [Genbank:AF276753], *Xenopus laevis* BXR α [Genbank:BC041187], *Xenopus laevis* BXR β [Genbank:AF305201], *Xenopus tropicalis* PXR [Ensembl, <http://www.ensembl.com:ENSXETT00000039109>], zebrafish PXR [Genbank:AF454673, Genbank:AF502918], and *Ciona intestinalis* VDR/PXR [Genbank:BR000137].

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