Baker et al.:

Identifying Candidate Reference Chemicals for *In Vitro* Testing of the Retinoid Pathway for Predictive Developmental Toxicity

Supplementary Data

Abbreviations
AC50, concentration at which there is 50% activity; CAS RN, Chemical Abstracts Service Registry Number; Chem Ct, chemical count; DSSTOXID, EPA DSSTox database identification number; N/A, not applicable; PDB, ID: Protein Data Bank Identification Number; PMID, PubMed Identifier; Year Dep, year deposited

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Tab. S1: Summary of Protein Data Bank records for retinol binding protein (RBP) serum/plasma

PDB ID	Structure title	Year Dep	PMID	Ligands used
1AQB	RETINOL-BINDING PROTEIN (RBP) FROM PIG PLASMA	1997	9757135	CADMIUM ION / RETINOL
1BRP	CRYSTAL STRUCTURE OF THE TRIGONAL FORM OF HUMAN PLASMA RETINOL-BINDING PROTEIN AT 2.5 ANGSTROMS RESOLUTION	1992	8464067	RETINOL
1BRQ	CRYSTAL STRUCTURE OF THE TRIGONAL FORM OF HUMAN PLASMA RETINOL-BINDING PROTEIN AT 2.5 ANGSTROMS RESOLUTION	1992	8464067	N/A
1ERB	THE INTERACTION OF N-ETHYL RETINAMIDE WITH PLASMA RETINOL-BINDING PROTEIN (RBP) AND THE CRYSTAL STRUCTURE OF THE RETINOID-RBP COMPLEX AT 1.9 ANGSTROMS RESOLUTION	1993	8227049	N-ETHYL RETINAMIDE
1FEL	CRYSTALLOGRAPHIC STUDIES ON COMPLEXES BETWEEN RETINOIDS AND PLASMA RETINOL-BINDING PROTEIN	1994	7961949	N-(4-HYDROXYPHENYL)ALL-TRANS RETINAMIDE

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1FEM	CRYSTALLOGRAPHIC STUDIES ON COMPLEXES BETWEEN RETINOIDS AND PLASMA RETINOL-BINDING PROTEIN	1994	7961949	RETINOIC ACID
1FEN	CRYSTALLOGRAPHIC STUDIES ON COMPLEXES BETWEEN RETINOIDS AND PLASMA RETINOL-BINDING PROTEIN	1994	7961949	ALL-TRANS AXEROPHTHENE
1HBP	CRYSTAL STRUCTURE OF LIGANDED AND UNLIGANDED FORMS OF BOVINE PLASMA RETINOL-BINDING PROTEIN	1993	8496140	RETINOL
1HBQ	CRYSTAL STRUCTURE OF LIGANDED AND UNLIGANDED FORMS OF BOVINE PLASMA RETINOL-BINDING PROTEIN	1993	8496140	N/A
1IIU	Chicken plasma retinol-binding protein (RBP)	2001	11738088	CADMIUM ION / RETINOL
1JYD	Crystal Structure of Recombinant Human Serum Retinol-Binding Protein at 1.7 A Resolution	2001	11604536	GLYCEROL
1JYJ	Crystal Structure of a Double Variant (W67L/W91H) of Recombinant Human Serum Retinol-binding Protein at 2.0 A Resolution	2001	11604536	GLYCEROL
1KT3 - 1KT7	Crystal structure of bovine holo-RBP at pH 2.0	2002	12787682	RETINOL
1OO2	Crystal structure of transthyretin from Sparus aurata	2003	14644428	CADMIUM ION
1RBP	CRYSTALLOGRAPHIC REFINEMENT OF HUMAN SERUM RETINOL BINDING PROTEIN AT 2 ANGSTROMS RESOLUTION	1990	2217163	RETINOL
1RLB	RETINOL BINDING PROTEIN COMPLEXED WITH TRANSTHYRETIN	1995	7754382	RETINOIC ACID
1THC	CRYSTAL STRUCTURE DETERMINATION AT 2.3A OF HUMAN TRANSTHYRETIN-3',5'-DIBROMO-2',4,4',6-TETRA-HYDROXYAURONE COMPLEX	1992	1631168	3',5'-DIBROMO-2',4,4',6'-TETRAHYDROXY AURONE
1TTR	TRANSTHYRETIN-V/122/I CARDIOMYOPATHIC MUTANT	1996	15299606	N/A
1TYR	TRANSTHYRETIN COMPLEX WITH RETINOIC ACID	1995	8536704	(9cis)-retinoic acid
2WQ9	Crystal Structure of RBP4 bound to Oleic Acid	2009	N/A	CHLORIDE ION / GLYCEROL / OLEIC ACID
2WQA	Complex of TTR and RBP4 and Oleic Acid	2009	N/A	OLEIC ACID / SULFATE ION
2WR6	Structure of the complex of RBP4 with linoleic acid	2009	N/A	(11E,13E,15Z)-OCTADECA-11,13,15-TRIENOIC ACID / CHLORIDE ION
3BSZ	Crystal structure of the transthyretin-retinol binding protein-Fab complex	2007	7754382/ 10052934 / 10089423 / 19021760	RETINOL
3FMZ	Crystal Structure of Retinol-Binding Protein 4 (RBP4) in complex with non-retinoid ligand	2008	19147488	2-[({4-[2-(trifluoromethyl)phenyl]piperidin-1-yl}carbonyl)amino]benzoic acid (A1120)
3HJ0	Transthyretin in complex with a covalent small molecule kinetic stabilizer	2009	20081815	3-SULFINOALANINE / 4-fluorophenyl 3-[(E)-2-(4-hydroxy-3,5-dimethylphenyl)ethenyl]benzoate
4O9S	Crystal structure of Retinol-Binding Protein 4 (RBP4) in complex with a non-retinoid ligand	2014	24835984	1,2-ETHANEDIOL / 1-[4-(8lambda~4~-cyclopenta[4,5]thieno[2,3-d]pyrimidin-4-yl)piperazin-1-yl]-2-[2-(trifluoromethyl)phenyl]ethanone / CHLORIDE ION / DI(HYDROXYETHYL)ETHER
4PSQ	Crystal Structure of Retinol-Binding Protein 4 (RBP4) in complex with a non-retinoid ligand	2014	24835984	(1-benzyl-1H-imidazol-4-yl)[4-(2-chlorophenyl)piperazin-1-yl]methanone / 1,2-ETHANEDIOL / PHOSPHATE ION
5NTY	Structure of non-fluorescent human plasma RBP4	2017	29414511	CHLORIDE ION / PALMITIC ACID
5NU2	Structure of non-fluorescent human urine RBP4	2017	29414511	CHLORIDE ION / PALMITIC ACID
5NU6	Structure of non-fluorescent human amniotic fluid RBP4	2017	29414511	CHLORIDE ION / PALMITIC ACID
5NU7	Structure of human holo plasma RBP4	2017	29414511	CHLORIDE ION / RETINOL
5NU8	Structure of human urine RBP4 saturated with palmitate	2017	29414511	CHLORIDE ION / PALMITIC ACID
5NU9	Structure of human amniotic fluid RBP4 saturated with palmitate	2017	29414511	CHLORIDE ION / PALMITIC ACID

5NUA	Structure of human urine RBP4 saturated with laurate	2017	29414511	CHLORIDE ION / LAURIC ACID
5NUB	Structure of human amniotic fluid RBP4 saturated with laurate	2017	29414511	CHLORIDE ION / LAURIC ACID

Tab. S2: Summary of ChEMBL entries for retinol binding protein (RBP) serum/plasma

Assay ID	Chem Ct	Assay Description	PMID
CHEMBL3889136	123	TR-FRET Assay: TR-FRET assay for retinol-induced RBP4-TTR interaction Binding of a desired RBP4 antagonist displaces retinol and induces hindrance for RBP4-TTR interaction resulting in the decreased FRET signal.	N/A
CHEMBL3889135	124	Scintillation Proximity Binding Assay: Untagged human RBP4 purified from urine of tubular proteinuria patients was purchased from Fitzgerald Industries International. It was biotinylated using the EZ-Link Sulfo-NHS-LC-Biotinylation kit from Pierce following the manufacturer's recommendations. Binding experiments were performed in 96-well plates (OptiPlate, PerkinElmer) in a final assay volume of 100 ul per well in SPA buffer (IX PBS, pH 7.4, 1 mM EDTA, 0.1% BSA, 0.5% CHAPS).	N/A
CHEMBL3705730	17	Binding Assay: Streptavidin (20 ul) (10 ug/ml Streptavidin type II (Wako Pure Chemical Industries, Ltd.), 10 mM Tris-HCl (pH 7.5), 10 mM NaCl) was added to a 384 well black plate (Nunc MaxiSorp, Thermo Fisher Scientific Inc.), and the plate was subjected to centrifugation (1000 rpm, 1 min) and coated overnight at 4 C.	N/A
CHEMBL3705134	15	Binding Assay: The action of the compound of the present invention to inhibit binding of RBP4 and retinol and TTR was evaluated using the Retinol-RBP4-TTR ELISA (human-type ELISA) system.	N/A
CHEMBL3594968	35	Inhibition of retinol-induced interaction of bacterially expressed MBP-tagged RBP4 (unknown origin) with Eu3+ cryptate labeled TTR by HTRF assay	26181715
CHEMBL3594967	36	Displacement of [3H]-retinol from RBP4 (unknown origin) by scintillation proximity assay	26181715
CHEMBL3380010	35	Antagonist activity at maltose binding protein-tagged RBP4 (unknown origin) expressed in Escherichia coli assessed as inhibition of retinol-induced protein/transthyretin interaction by HTRF assay	25210858
CHEMBL3380009	35	Displacement of [3H]retinol from biotinylated human RBP4 by scintillation proximity assay	25210858
CHEMBL3291833	26	Inhibition of human recombinant RBP4-transthyretin interaction by FRET analysis	24835984
CHEMBL3291832	33	Displacement of [3H]-retinol from human recombinant RBP4 by scintillation proximity assay	24835984
CHEMBL1804573	7	Binding affinity to immobilized His-tagged recombinant human sRBP assessed as inhibition of sRBP and detergent treated HEK293 membrane interaction at 100 uM after 1 hr by surface plasmon resonance assay	21591606
CHEMBL1804572	2	Antagonist activity at His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of sRBP-TTR protein interaction after 2 hr by surface plasmon resonance assay	21591606
CHEMBL1804571	7	Antagonist activity at His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of ROH-sRBP-TTR protein interaction after 2 hr by TR-FRET assay relative to control	21591606
CHEMBL1804187	7	Antagonist activity at His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of ROH-sRBP-TTR protein interaction after 2 hr by TR-FRET assay	21591606
CHEMBL1804186	1	Binding affinity to His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of sRBP-TTR protein interaction at 100 uM after 1 hr by SDS-PAGE and silver staining method relative to 10 uM ROH	21591606
CHEMBL1804185	47	Binding affinity to His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of sRBP-TTR protein interaction after 1 hr by SDS-PAGE and silver staining method	21591606
CHEMBL1804184	21	Binding affinity to His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as disruption of sRBP-TTR protein interaction at 1 to 100 uM after 1 hr by SDS-PAGE and silver staining method	21591606
CHEMBL1804183	8	Binding affinity to His-tagged recombinant human sRBP expressed in Escherichia coli BL21(DE3) assessed as apparent dissociation constant after 5 mins by fluorescence spectrophotometric analysis	21591606

Tab. S3: Protein Data Bank entries for STRA6

PDB ID	Structure title	Year Dep	PMID	Ligands used
5K8Q	Crystal Structure of Calcium-loaded Calmodulin in complex with STRA6 CaMBP2-site peptide.	2016	27563101	IMIDAZOLE /CALCIUM ION / AMINO GROUP / ACETYL GROUP
5SY1	Structure of the STRA6 receptor for retinol uptake in complex with calmodulin	2016	27563101	CALCIUM ION / CHOLESTEROL

Tab. S4: Summary of Protein Data Bank records for Cellular Retinol Binding Protein (CRBP)

PDB link	Structure title	PMID	Year Dep	Ligands used
1B4M	NMR STRUCTURE OF APO CELLULAR RETINOL-BINDING PROTEIN II, 24 STRUCTURES	10047490	1998	N/A
1CBQ	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	6-(2,3,4,5,6,7-HEXAHYDRO-2,4,4-TRIMETHYL-1-METYLENEINDEN-2-YL)-3-METHYLHEXA-2,4-DIENOIC ACID / PHOSPHATE ION
1CBR	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	RETINOIC ACID
1CBS	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	RETINOIC ACID
1CRB	CRYSTALLOGRAPHIC STUDIES ON A FAMILY OF CELLULAR LIPOPHILIC TRANSPORT PROTEINS. REFINEMENT OF P2 MYELIN PROTEIN AND THE STRUCTURE DETERMINATION AND REFINEMENT OF CELLULAR RETINOL-BINDING PROTEIN IN COMPLEX WITH ALL-TRANS-RETINOL	7683727	1993	CADMIUM ION / RETINOL
1EII	NMR STRUCTURE OF HOLO CELLULAR RETINOL-BINDING PROTEIN II	10884357	2000	RETINOL
1GGL	HUMAN CELLULAR RETINOL BINDING PROTEIN III	11274389	2000	N/A
1JBH	Solution structure of cellular retinol binding protein type-I in the ligand-free state	11934897	2001	N/A
1KGL	Solution structure of cellular retinol binding protein type-I in complex with all-trans-retinol	11934897	2001	RETINOL
1KQW , 1KQX	Crystal structure of holo-CRBP from zebrafish	12162964	2002	RETINOL
1LPJ	Human cRBP IV	12177003	2002	N/A
1MX7	Two homologous rat cellular retinol-binding proteins differ in local structure and flexibility	12850148	2002	N/A
1MX8	Two homologous rat cellular retinol-binding proteins differ in local structure and flexibility	12850148	2002	RETINOL
1OPA	THE CRYSTAL STRUCTURES OF HOLO-AND APO-CELLULAR RETINOL BINDING PROTEIN II	8487303	1992	N/A
1OPB	THE CRYSTAL STRUCTURES OF HOLO-AND APO-CELLULAR RETINOL BINDING PROTEIN II	8487303	1992	RETINAL
1PMP	CRYSTALLOGRAPHIC STUDIES ON A FAMILY OF CELLULAR LIPOPHILIC TRANSPORT PROTEINS. REFINEMENT OF P2 MYELIN PROTEIN AND THE STRUCTURE DETERMINATION AND REFINEMENT OF CELLULAR RETINOL-BINDING PROTEIN IN COMPLEX WITH ALL-TRANS-RETINOL	7683727	1993	OLEIC ACID
2RCQ	Crystal structure of human apo Cellular Retinol Binding Protein II (CRBP-II)	18076076	2007	L(+)-TARTARIC ACID / SULFATE ION
2RCT	Crystal structure of human holo cellular retinol-binding protein II (CRBP-II)	18076076	2007	L(+)-TARTARIC ACID / RETINOL / SULFATE ION
3CR6	Crystal Structure of the R132K:R111L:A32E Mutant of Cellular Retinoic Acid Binding Protein Type II Complexed with C15-aldehyde (a retinal analog) at 1.22 Angstrom resolution.	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3CWK	Crystal Structure of the R132K:Y134F:R111L:T54V:L121E Mutant of Cellular Retinoic Acid Binding Protein Type II in Complex with All-trans-Retinoic Acid at 1.57 Angstroms Resolution	19018099	2008	RETINOIC ACID / SULFATE ION
3D95	Crystal Structure of the R132K:Y134F:R111L:L121E:T54V	19018099	2008	N/A

	Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II at 1.20 Angstroms Resolution			
3D96	Crystal Structure of the R132K:Y134F Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II at 1.71 Angstroms Resolution	19018099	2008	ACETATE ION
3D97	Crystal Structure of the R132K:R111L:L121E Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II At 1.50 Angstroms Resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL / SODIUM ION
3F8A	Crystal Structure of the R132K:R111L:L121E:R59W Mutant of Cellular Retinoic Acid-Binding Protein Type II Complexed with C15-aldehyde (a retinal analog) at 1.95 Angstrom resolution.	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene / 2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3F9D	Crystal structure of the R132K:R111L:T54E mutant of cellular retinoic acid-binding protein II complexed with C15-aldehyde (a retinal analog) at 2.00 angstrom resolution	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3FA6	Crystal structure of the R132K:Y134F:R111L:L121D:T54V mutant of cellular retinoic acid-binding protein II complexed with C15-aldehyde (a retinal analog) at 1.54 angstrom resolution	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3FA7	Crystal structure of the apo R132K:R111L:L121E:R59E mutant of cellular retinoic acid-binding protein II at 1.90 angstrom resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3FA8	Crystal structure of the apo R132K:Y134F:R111L:L121E mutant of cellular retinoic acid-binding protein II at 1.78 angstrom resolution	N/A	2008	N/A
3FA9	Crystal structure of the apo R132K:Y134F:R111L:L121D mutant of cellular retinoic acid-binding protein II at 1.94 angstrom resolution	N/A	2008	ACETATE ION
3FEK	Crystal structure of the R132K:Y134F:R111L:L121D:T54V mutant of cellular retinoic acid-binding protein II at 1.51 angstrom resolution	N/A	2008	ACETATE ION / DI(HYDROXYETHYL)ETHER
3FEL	Crystal structure of the R132K:R111L:T54E mutant of cellular retinoic acid-binding protein II at 1.85 angstrom resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3FEN	Crystal structure of the R132K:R111L:A32E mutant of cellular retinoic acid-binding protein II at 1.56 angstrom resolution	N/A	2008	CHLORIDE ION
3FEP	Crystal structure of the R132K:R111L:L121E:R59W-CRABPII mutant complexed with a synthetic ligand (merocyanin) at 2.60 angstrom resolution.	25534273	2008	(2E,4E,6E)-3-methyl-6-(1,3,3-trimethyl-1,3-dihydro-2H-indol-2-ylidene)hexa-2,4-dienal / 2-(N-MORPHOLINO)-ETHANESULFONIC ACID
3HX3	Crystal structure of CRALBP mutant R234W	19846785	2009	RETINAL / SELENOMETHIONINE
3HY5	Crystal structure of CRALBP	19846785	2009	L(+)-TARTARIC ACID / RETINAL
3I17	Crystal structure of the apo R132K:L121E mutant of cellular retinoic acid-binding protein II at 1.68 angstrom resolution	19603486	2009	N/A
4EDE	Crystal Structure of the Q108K:K40L:T51V:T53C:Y19W:R58W:T29L:A33W Mutant of Cellular Retinol Binding Protein Type II in Complex with All-trans-Retinal at 1.4 Angstrom Resolution	23224553	2012	ACETATE ION / RETINAL
4EEJ	Crystal Structure of the Q108K:K40L:T51V:T53C:Y19W:R58W:T29L:Q4R Mutant of Cellular Retinol Binding Protein Type II in Complex with	23224553	2012	ACETATE ION / RETINAL

	All-trans-Retinal at 1.5 Angstrom Resolution			
4EFG	Crystal Structure of the Q108K:K40L:T51V:T53C:Y19W:R58W:T29L Mutant of Cellular Retinol Binding Protein Type II in Complex with All-trans-Retinal at 1.58 Angstrom Resolution	23224553	2012	ACETATE ION / RETINAL
4EXZ	Crystal Structure of the Q108K:K40L Mutant of Cellular Retinol Binding Protein Type II in Complex with All-trans-Retinal at 1.7 Angstrom Resolution	23224553	2012	ACETATE ION / RETINAL
4GKC	Crystal structure of Q108K:K40L:T51V:T53C:R58W:T29L:Y19W:Q4A mutant of cellular retinol binding protein II complex with all-trans-retinal at 1.33	23224553	2012	RETINAL
4HIQ	The Structure of V122I Mutant Transthyretin in Complex with AG10	23716704	2012	3-[3-(3,5-dimethyl-1H-pyrazol-4-yl)propoxy]-4-fluorobenzoic acid
4HIS	The Structure of V122I Mutant Transthyretin in Complex with Tafamidis	23716704	2012	2-(3,5-dichlorophenyl)-1,3-benzoxazole-6-carboxylic acid
4QYN	The Crystal Structures of holo-wt human Cellular Retinol Binding protein II (hCRBPII) bound to Retinol	25478840	2014	ACETATE ION / RETINOL
4QYP	The Crystal Structures of holo-wt human Cellular Retinol Binding protein II (hCRBPII) bound to Retinal	25478840	2014	ACETATE ION / RETINAL
4QZT	Crystal Structure of wild type Human Cellular Retinol Binding Protein II (hCRBPII) bound to retinol at 7 KeV beam energy	25478840	2014	ACETATE ION / RETINOL
4QZU	Crystal Structure of wild type Human Cellular Retinol Binding Protein II (hCRBPII) bound to retinol at 11 KeV beam energy	25478840	2014	ACETATE ION / GLYCEROL / RETINOL
4RUU	Crystal structure of the Q108K:K40L mutant of human Cellular Retinol Binding ProteinII in complex with All-trans-Retinal after 24 hour incubation at 1.4 Angstrom Resolution	23224553	2014	ACETATE ION / RETINAL
4ZCB	Human CRBPII mutant - Y60W dimer	27524203	2015	N/A
4ZGU	Crystal structure of monomer Y60W hCRBPII	27524203	2015	ACETATE ION
4ZH6	Crystal Structure of the Domain-Swapped Dimer Y60L mutant of Human Cellular Retinol Binding Protein II	27524203	2015	ACETATE ION
4ZH9	Crystal Structure of the Domain-Swapped Dimer Wild-Type of Human Cellular Retinol Binding Protein II	27524203	2015	N/A
4ZJ0	The crystal structure of monomer Q108K:K40L:Y60W CRBPII bound to all-trans-retinal	27524203	2015	ACETATE ION / RETINAL
4ZR2	Crystal Structure of the Domain-Swapped Dimer K40L:Q108K:Y60W mutant of Human Cellular Retinol Binding Protein II	27524203	2015	ACETATE ION / RETINAL
5DG4	Crystal structure of monomer human cellular retinol binding protein II-Y60L	27524203	2015	ACETATE ION
5DPQ	Crystal Structure of E72A mutant of domain swapped dimer Human Cellular Retinol Binding Protein	27524203	2015	ACETATE ION
5F58	Crystal structure of the Q108K:K40L:T51V:R58F mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal after 24 hours of incubation at 1.54 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5F6B	Crystal structure of the Q108K:K40L:T51V:R58Y:Y19W mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal at 1.3 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5F7G	Crystal structure of the Q108K:K40L:T51V:R58Y:Y19W:Q38L mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal at 1.48 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5FAZ	Crystal structure of the Q108K:K40L:T51V mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal after 24 hours of incubation at 1.4 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5FEN	Crystal structure of the Q108K:K40L:T53C mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal after 24 hours of incubation at 1.55 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5FFH	Crystal structure of the Q108K:K40L:T51V:R58W:Y19W mutant of human Cellular Retinol Binding Protein II in complex with All-trans-Retinal at 1.68 Angstrom Resolution	N/A	2015	ACETATE ION / RETINAL
5H8T	Crystal structure of human cellular retinol binding protein 1 in complex with all-trans-retinol	26900151	2015	RETINOL

5H9A	Crystal structure of the Apo form of human cellular retinol binding protein 1	26900151	2015	2-[BIS-(2-HYDROXY-ETHYL)-AMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
5HA1	Crystal structure of human cellular retinol binding protein 1 in complex with retinylamine	26900151	2015	(2~{E},4~{E},6~{E},8~{E})-3,7-dimethyl-9-(2,6,6-trimethylcyclohexen-1-yl)nona-2,4,6,8-tetraen-1-amine
5HBS	Crystal structure of human cellular retinol binding protein 1 in complex with all-trans-retinol at 0.89 angstrom.	26900151	2016	RETINOL
5LJB	Crystal structure of holo human CRBP1	28057518	2016	RETINOL
5LJC	Crystal structure of holo human CRBP1	28057518	2016	RETINOL / SODIUM ION
5LJD	Crystal structure of holo human CRBP1/K40L mutant	28057518	2016	RETINOL / SODIUM ION
5LJE	Crystal structure of holo human CRBP1/K40L,Q108L mutant	28057518	2016	RETINOL / SODIUM ION
5LJG	Crystal structure of holo human CRBP1	28057518	2016	PALMITIC ACID
5LJH	Crystal structure of human apo CRBP1/K40L mutant	28057518	2016	SODIUM ION
5LJK	Crystal structure of human apo CRBP1	28057518	2016	SODIUM ION
5U6G	Crystal Structure of the holo Domain-Swapped Dimer mutant Q108K:K40D Human Cellular Retinol Binding Protein II bound with all trans retinal	N/A	2016	RETINAL
6AT8	1.1 Angstrom Resolution Structure of Human Cellular Retinol-Binding Protein IV	N/A	2017	DI(HYDROXYETHYL)ETHER / GLYCEROL
6BTH	Crystal structure of human cellular retinol binding protein 2 (CRBP2) in complex with 2-arachidonoylglycerol (2-AG)	N/A	2017	1,3-dihydroxypropan-2-yl (5Z,8Z,11Z,14Z)-icosa-5,8,11,14-tetraenoate / DI(HYDROXYETHYL)ETHER
6BTI	Crystal structure of human cellular retinol binding protein 2 (CRBP2) in complex with N-arachidonoylethanolamine (AEA)	N/A	2017	(5Z,8Z,11Z,14Z)-N-(2-hydroxyethyl)icosa-5,8,11,14-tetraenamide / DI(HYDROXYETHYL)ETHER
6C7Z	Crystal structure of the Q108K:K40L:T51V:R58F mutant of human Cellular Retinol Binding Protein II in complex with synthetic Ligand Julolidine	29645331	2018	(2E,4E)-3-methyl-5-(2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)penta-2,4-dienal / ACETATE ION
6E50	Crystal structure of the apo domain-swapped dimer Q108K:K40L:T51F mutant of human Cellular Retinol Binding Protein II	31557439	2018	ACETATE ION
6E51	Crystal structure of the apo domain-swapped dimer Q108K:K40L:T51W mutant of human cellular retinol binding protein II	31557439	2018	N/A
6E5E	Crystal structure of the apo domain-swapped dimer Q108K:T51D mutant of human cellular retinol binding protein II	31557439	2018	ACETATE ION
6E5L	Crystal structure of human cellular retinol binding protein 1 in complex with abnormal-cannabidiol (abn-CBD)	30721022	2018	(1'R,2'R)-5'-methyl-6-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro[1,1'-biphenyl]-2,4-diol
6E5Q	Crystal structure of the apo domain-swapped dimer Q108K:T51D:A28H mutant of human Cellular Retinol Binding Protein II	31557439	2018	ACETATE ION
6E5R	Crystal structure of the apo domain-swapped dimer Q108K:T51D:A28C mutant of human Cellular Retinol Binding Protein II	31557439	2018	ACETATE ION / GLYCEROL
6E5S	Crystal structure of holo retinal-bound domain-swapped dimer Q108K:T51D mutant of human Cellular Retinol Binding Protein II	31557439	2018	RETINAL
6E5T	Crystal structure of human cellular retinol binding protein 1 in complex with abnormal-cannabidiorcin (Abn-CBDO)	30721022	2018	(1'R,2'R)-5',6-dimethyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro[1,1'-biphenyl]-2,4-diol
6E5W	Crystal structure of human cellular retinol binding protein 3 in complex with abnormal-cannabidiol (abn-CBD)	30721022	2018	(1'R,2'R)-5'-methyl-6-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro[1,1'-biphenyl]-2,4-diol / GLYCEROL
6E6K	Crystal structure of human cellular retinol-binding protein 4 in complex with abnormal-cannabidiol (abn-CBD)	30721022	2018	(1'R,2'R)-5'-methyl-6-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-

				tetrahydro[1,1'-biphenyl]-2,4-diol
6E6L	Crystal structure of the holo retinal-bound domain-swapped dimer Q108K:K40L:T51F:Y60A mutant of human cellular retinol binding protein II	31557439	2018	ACETATE ION / RETINAL
6E6M	Crystal structure of human cellular retinol-binding protein 1 in complex with cannabidiorcin (CBDO)	30721022	2018	(1'R,2'R)-4,5'-dimethyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro[1,1'-biphenyl]-2,6-diol
6E7M	Crystal structure of the holo retinal-bound domain-swapped dimer Q108K:T51D:A28C mutant of human Cellular Retinol Binding Protein II	31557439	2018	ACETATE ION / GLYCEROL / RETINAL
6MCU	Crystal structure of the holo retinal-bound domain-swapped dimer Q108K:T51D:A28H mutant of human Cellular Retinol Binding Protein II	31557439	2018	GLYCEROL / RETINAL
6MCV	Crystal Structure of Holo Retinal-Bound Domain-Swapped Dimer of Wild Type Human Cellular Retinol Binding Protein II	31557439	2018	RETINAL
6MKV	Crystal structure of Retinal-bound holo Q108K:K40L:T51W domain-swapped dimer of human cellular retinol binding protein 2	31557439	2018	ACETATE ION / GLYCEROL / RETINAL
6MLB	Crystal structure of the holo retinal-bound domain-swapped dimer Q108K:K40L:T51F mutant of human cellular retinol binding protein II	31557439	2018	ACETATE ION / GLYCEROL / RETINAL
6ON5	Crystal Structure of the Zn-bound Domain-Swapped Dimer Q108K:T51D:A28C:L36C:F57H Mutant of Human Cellular Retinol Binding Protein II	31557439	2019	ZINC ION
6ON7	Crystal Structure of Apo Domain-Swapped Dimer Q108K:T51D:A28C:L36C Mutant of Human Cellular Retinol Binding Protein II	31557439	2019	N/A
6ON8	Crystal Structure of the Reduced Form of Apo Domain-Swapped Dimer Q108K:T51D:A28C:L36C:F57H Mutant of Human Cellular Retinol Binding Protein II	31557439	2019	N/A

Tab. S5: Summary of Protein Data Bank results for Cellular Retinoic Acid Binding Proteins (CRABP1 and CRABP2)

PDB link	Structure title	PMID	Year Dep	Ligands used
1CBI	APO-CELLULAR RETINOIC ACID BINDING PROTEIN I	7563063	1995	N/A
1CBQ	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	6-(2,3,4,5,6,7-HEXAHYDRO-2,4,4-TRIMETHYL-1-METYLENEINDEN-2-YL)-3-METHYLHEXA-2,4-DIENOIC ACID / PHOSPHATE ION
1CBR	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	RETINOIC ACID
1CBS	CRYSTAL STRUCTURE OF CELLULAR RETINOIC-ACID-BINDING PROTEINS I AND II IN COMPLEX WITH ALL-TRANS-RETINOIC ACID AND A SYNTHETIC RETINOID	7704533	1994	RETINOIC ACID
1XCA	APO-CELLULAR RETINOIC ACID BINDING PROTEIN II	9600845	1996	N/A
1BLR	NMR SOLUTION STRUCTURE OF HUMAN CELLULAR RETINOIC ACID BINDING PROTEIN-TYPE II, 22 STRUCTURES	9737849	1998	N/A
1BM5	THE SOLUTION STRUCTURE OF A SITE-DIRECTED MUTANT (R111M) OF HUMAN CELLULAR RETIONIC ACID BINDING PROTEIN-TYPE II, NMR, 31 STRUCTURES	9737883	1998	N/A
2CBR	CELLULAR RETINOIC ACID BINDING PROTEIN I IN COMPLEX WITH A RETINOBENZOIC ACID (AM80)	10531482	1999	4-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)carbamoyl]benzoic acid
2CBS	CELLULAR RETINOIC ACID BINDING PROTEIN II IN COMPLEX WITH A SYNTHETIC	10531482	1999	3-METHYL-7-(5,5,8,8-TETRAMETHYL-5,6,7,8-

	RETINOIC ACID (RO-13 6307)			TETRAHYDRO-NAPHTHALEN-2-YL) - OCTA-2,4,6-TRIENOIC ACID
3CBS	CELLULAR RETINOIC ACID BINDING PROTEIN II IN COMPLEX WITH A SYNTHETIC RETINOIC ACID (RO-12 7310)	10531482	1999	(2E,4E,6E,8E)-9-(4-hydroxy-2,3,6-trimethylphenyl)-3,7-dimethylnona-2,4,6,8-tetraenoic acid
2FR3	Crystal Structure of Cellular Retinoic Acid Binding Protein Type II in Complex with All-Trans-Retinoic Acid at 1.48 Angstroms Resolution	16979656	2006	ACETATE ION / RETINOIC ACID
2FRS	Crystal structure of the f15w mutant of apo-cellular retinoic acid binding protein type ii at 1.51 angstroms resolution	16979656	2006	SODIUM ION /
2FS6	Crystal Structure of Apo-Cellular Retinoic Acid Binding Protein Type II At 1.35 Angstroms Resolution	16979656	2006	ACETATE ION / CHLORIDE ION / SODIUM ION
2FS7	Crystal Structure of Apo-Cellular Retinoic Acid Binding Protein Type II At 1.55 Angstroms Resolution	16979656	2006	ACETATE ION / CHLORIDE ION
2G78	Crystal Structure of the R132K:Y134F Mutant of Cellular Retinoic Acid Binding Protein Type II in Complex with All-Trans-Retinoic Acid at 1.70 Angstroms Resolution	17447762	2006	RETINOIC ACID / SODIUM ION
2G79	Crystal Structure of the R132K:Y134F Mutant of Cellular Retinoic Acid Binding Protein Type II in Complex with All-Trans-Retinal at 1.69 Angstroms Resolution	17447762	2006	RETINAL / SODIUM ION / SULFATE ION
2G7B	Crystal Structure of the R132K:R111L:L121E mutant of Cellular Retinoic Acid Binding Protein Type II In Complex With All-Trans-Retinal At 1.18 Angstroms Resolution	17447762	2006	ALL-TRANS AXEROPHTHENE / SODIUM ION
3CWK	Crystal Structure of the R132K:Y134F:R111L:T54V:L121E Mutant of Cellular Retinoic Acid Binding Protein Type II in Complex with All-trans-Retinoic Acid at 1.57 Angstroms Resolution	19018099	2008	RETINOIC ACID / SULFATE ION
3D95	Crystal Structure of the R132K:Y134F:R111L:L121E:T54V Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II at 1.20 Angstroms Resolution	19018099	2008	N/A
3D96	Crystal Structure of the R132K:Y134F Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II at 1.71 Angstroms Resolution	19018099	2008	ACETATE ION /
3I17	Crystal structure of the apo R132K:L121E mutant of cellular retinoic acid-binding protein II at 1.68 angstrom resolution	19603486	2009	N/A
4I9R 4I9S 4M6S 4M7M	Crystal Structure of a Mutant of the Cellular Retinoic Acid Binding Protein Type II in Complex with All-Trans Retinal at various conditions	24059243	2012	RETINAL
3FEP 4QGV 4QGW 4QGX	Crystal structure of a CRABPII mutant complexed with a synthetic ligand (merocyanin) at various conditions	25534273	2008	(2E,4E,6E)-3-methyl-6-(1,3,3-trimethyl-1,3-dihydro-2H-indol-2-ylidene)hexa-2,4-dienal / 2-(N-MORPHOLINO)-ETHANESULFONIC ACID
5HZQ	Crystal structure of cellular retinoic acid binding protein 2 (CRABP2)-aryl fluorosulfate covalent conjugate	27191344	2016	4'-[(3,6,9,12-tetraoxapentadec-14-yn-1-yl)oxy][1,1'-biphenyl]-4-yl sulfurofluoridate / GLYCEROL
4YBP 4YFR 4YBU 4YGG 4YCE 4YGH 4YCH 4YGZ 4YDA 4YH0	Crystal structure of the mutant of human cellular retinoic acid binding protein II with retinal – various conditions	27310917	2015	RETINAL

4YDB 4YKM 4YFP 4YKO 4YFQ				
6MOP 6MQI 6MOQ 6MQJ 6MOR 6MQW 6MOV 6MQX 6MOX 6MQY 6MPK 6MQZ 6MR0	Crystal Structure of the All-trans Retinal-Bound Mutant of Human Cellular Retinoic Acid Binding Protein II – various conditions	30580520	2018	RETINAL
6HKR	Human Cellular Retinoic Acid Binding Protein II (CRABPII) with bound synthetic retinoid DC271.	30613343	2018	1,2-ETHANEDIOL / 4-[2-(4,4-dimethyl-1-propan-2-yl-2,3-dihydroquinolin-6-yl)ethynyl]benzoic acid / GLYCEROL / TETRAETHYLENE GLYCOL
5OGB	Human Cellular Retinoic Acid Binding Protein II (CRABPII) with bound synthetic retinoid DC360.	30707838	2017	4-[2-(4,4-dimethyl-1-propan-2-yl-quinolin-6-yl)ethynyl]benzoic acid
3CR6	Crystal Structure of the R132K:R111L:A32E Mutant of Cellular Retinoic Acid Binding Protein Type II Complexed with C15-aldehyde (a retinal analog) at 1.22 Angstrom resolution.	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3D97	Crystal Structure of the R132K:R111L:L121E Mutant of Apo-Cellular Retinoic Acid Binding Protein Type II At 1.50 Angstroms Resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL / SODIUM ION
3F8A	Crystal Structure of the R132K:R111L:L121E:R59W Mutant of Cellular Retinoic Acid-Binding Protein Type II Complexed with C15-aldehyde (a retinal analog) at 1.95 Angstrom resolution.	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene / 2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3F9D	Crystal structure of the R132K:R111L:T54E mutant of cellular retinoic acid-binding protein II complexed with C15-aldehyde (a retinal analog) at 2.00 angstrom resolution	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3FA6	Crystal structure of the R132K:Y134F:R111L:L121D:T54V mutant of cellular retinoic acid-binding protein II complexed with C15-aldehyde (a retinal analog) at 1.54 angstrom resolution	N/A	2008	1,3,3-trimethyl-2-[(1E,3E)-3-methylpenta-1,3-dien-1-yl]cyclohexene
3FA7	Crystal structure of the apo R132K:R111L:L121E:R59E mutant of cellular retinoic acid-binding protein II at 1.90 angstrom resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3FA8	Crystal structure of the apo R132K:Y134F:R111L:L121E mutant of cellular retinoic acid-binding protein II at 1.78 angstrom resolution	N/A	2008	N/A
3FA9	Crystal structure of the apo R132K:Y134F:R111L:L121D mutant of cellular retinoic acid-binding protein II at 1.94 angstrom resolution	N/A	2008	ACETATE ION /
3FEK	Crystal structure of the R132K:Y134F:R111L:L121D:T54V mutant of	N/A	2008	ACETATE ION / DI(HYDROXYETHYL)ETH

	cellular retinoic acid-binding protein II at 1.51 angstrom resolution			ER /
3FEL	Crystal structure of the R132K:R111L:T54E mutant of cellular retinoic acid-binding protein II at 1.85 angstrom resolution	N/A	2008	2-[3-(2-HYDROXY-1,1-DIHYDROXYMETHYL-ETHYLAMINO)-PROPYLAMINO]-2-HYDROXYMETHYL-PROPANE-1,3-DIOL
3FEN	Crystal structure of the R132K:R111L:A32E mutant of cellular retinoic acid-binding protein II at 1.56 angstrom resolution	N/A	2008	CHLORIDE ION
6AT8	1.1 Angstrom Resolution Structure of Human Cellular Retinol-Binding Protein IV	N/A	2017	DI(HYDROXYETHYL)ETHER / GLYCEROL
6MOW	Crystal Structure of the apo R111K:Y134F:T54V:R132Q:P39Y:R59Y:L121Q mutant of Human Cellular Retinoic Acid Binding Protein II at 2.3 Angstrom Resolution	N/A	2018	N/A
6NNX	Crystal Structure of the All-Trans Retinal-Bound R111K:Y134F:T54V:R132Q:P39Y:R59Y:L121M Mutant of Human Cellular Retinoic Acid Binding Protein II in the Dark at 1.87 Angstrom Resolution	N/A	2019	RETINAL
6NNY	Crystal Structure of the All-Trans Retinal-Bound R111K:Y134F:T54V:R132Q:P39E:R59Y:L121E Mutant of Human Cellular Retinoic Acid Binding Protein II in the Dark at 1.67 Angstrom Resolution	N/A	2019	RETINAL
6NOE	Crystal Structure of the All-Trans Retinal-Bound R111K:Y134F:T54V:R132Q:P39Y:R59Y:L121E:I63D Mutant of Human Cellular Retinoic Acid Binding Protein II in the Dark at 1.97 Angstrom Resolution	N/A	2019	RETINAL

Tab. S6: Summary of ChEMBL results for Cellular Retinoic Acid Binding Proteins (CRABP1 and CRABP2)

Assay ID	Chem Ct	Assay description	PMID
CHEMBL661352	10	Inhibition of chick skin Cytoplasmic retinoic acid binding protein at 100-fold excess ligand	8809153
CHEMBL661351	6	Tested for its ability to inhibit the binding of (all-E-)-RA to cytoplasmic retinoic acid-binding protein (CRABP) from chick skin	7799400
CHEMBL884347	1	Inhibition of [3H]ATRA binding to chick skin Cytoplasmic retinoic acid binding protein	8809153
CHEMBL665219	8	Inhibition of [3H]ATRA binding to chick skin Cytoplasmic retinoic acid binding protein	8809153
CHEMBL665218	7	Inhibition of binding to chick skin Cytoplasmic retinoic acid binding protein	7608895
CHEMBL662931	1	Concentration of compound required to inhibit binding of 2.5 uM [3H]all-trans-retinoic acid by 50% in chick	2738885
CHEMBL662930	1	Concentration of compound required to inhibit binding of 2.5 uM [3H]all-trans-retinoic acid by 50% in chick	2738885
CHEMBL662929	7	Concentration of compound required to inhibit binding of 2.5 uM [3H]all-trans-retinoic acid by 50% in chick	2738885
CHEMBL665905	7	Binding affinity for mouse Cytoplasmic retinoic acid binding protein type 2	7608895
CHEMBL875705	7	Inhibition of [3H]ATRA binding to murine Cytoplasmic retinoic acid binding protein (CRABP) type 2	8809153
CHEMBL665904	4	Inhibition of [3H]ATRA binding to murine Cytoplasmic retinoic acid binding protein (CRABP) type 2	8809153
CHEMBL665903	7	Binding affinity for mouse Cytoplasmic retinoic acid binding protein type 1	7608895
CHEMBL665902	9	Inhibition of [3H]ATRA binding to murine Cytoplasmic retinoic acid binding protein (CRABP) type 1	8809153
CHEMBL665901	1	Inhibition of [3H]ATRA binding to murine Cytoplasmic retinoic acid binding protein (CRABP) type 1	8809153
CHEMBL2182124	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human MCF7 cells assessed as reduction in CRABP2 level at 0.1 uM to 1 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2182123	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as reduction in CRABP2 level at 0.1 uM to 1 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2182119	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human IMR32 cells assessed as reduction in CRABP-2 level at 1 to 10 uM after 48 hrs by Western	21515062

		blot analysis	
CHEMBL2182118	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human IMR32 cells assessed as reduction in MycN level at 1 to 10 uM after 48 hrs by Western blot analysis	21515062
CHEMBL2188719	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 1000 uM by Western blot analysis	21515062
CHEMBL2188718	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 1 uM after 6 hrs by Western blot analysis in presence of MeBS	21515062
CHEMBL2188717	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 1 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2188716	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 1 uM after 6 hrs by Western blot analysis in presence of proteasome inhibitor MG132	21515062
CHEMBL2188715	2	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as formation of ternary complex by GST-pull down assay	21515062
CHEMBL2188714	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 1 uM after 6 hrs by Western blot analysis in presence of proteasome inhibitor lactacystin	21515062
CHEMBL2188713	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in cIAP1 degradation at 30 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2188712	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation after 6 hrs by Western blot analysis	21515062
CHEMBL2188711	2	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in cIAP1 degradation at 0.1 to 10 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2188710	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation at 0.1 to 10 uM after 6 hrs by Western blot analysis	21515062
CHEMBL2188708	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation after 12 hrs by Western blot analysis	21515062
CHEMBL2188707	1	Binding affinity to Flag-tagged cIAP1/CRABP2 expressed in human HT1080 cells assessed as induction in CRABP-2 degradation after 48 hrs by Western blot analysis	21515062
CHEMBL664300	2	Inhibition of [3H]-retinoic acid binding to Cellular retinoic acid-binding protein (CRABP) from chick embryo skin	12723955
CHEMBL664299	11	Inhibition of [3H]-retinoic acid binding to Cellular retinoic acid-binding protein (CRABP) from chick embryo skin	12723955
CHEMBL664298	1	Inhibition of [3H]-retinoic acid binding to Cellular retinoic acid-binding protein (CRABP) from chick embryo skin	12723955

Tab. S7: Summary of ChEMBL entries for CYP26

Assay ID	Chem Ct	Assay description	PMID
CHEMBL3789273	2	Inhibition of CYP26A1-mediated atRA metabolism in human HepG2 cells assessed as atRA level in cell media at 1 uM after 24 hrs by LC/MS-MS analysis (Rvb = 0.49 +/- 0.33 nM)	26918322
CHEMBL3789272	3	Inhibition of CYP26A1-mediated atRA metabolism in human HepG2 cells assessed as atRA level in cell media at 1 uM after 24 hrs in presence of 100 nM atRA by LC/MS-MS analysis relative to atRA-treated control	26918322
CHEMBL3789264	24	Inhibition of microsomal fraction of human CYP26A1 expressed in Sf9 cells using 9-cis-RA as substrate preincubated for 5 mins followed by NADPH addition measured after 1 min by HPLC analysis in presence of rat P450 reductase	26918322
CHEMBL3789258	3	Inhibition of CYP26A1 in human HepG2 cells assessed as upregulation of RARbeta mRNA expression at 1 uM after 24 hrs in presence of 100 nM atRA by RT-PCR method	26918322
CHEMBL3789257	3	Inhibition of CYP26A1 in human HepG2 cells assessed as upregulation of CYP26A1 mRNA expression at 1 uM after 24 hrs in presence of 100 nM atRA by RT-PCR method	26918322
CHEMBL3789256	3	Inhibition of CYP26A1-mediated atRA metabolism in human HepG2 cells assessed as atRA level in cell media at 1 uM after 24 hrs in presence of 100 nM atRA by LC/MS-MS analysis (Rvb = 13.2 +/- 0.14 nM)	26918322
CHEMBL3620667	2	Inhibition of CYP26A1-mediated ATRA metabolism in human HL60 cells	26365710

		assessed as ATRA level at 5 uM incubated for 96 hrs by HPLC method (Rvb = 1.21 uM)	
CHEMBL3620666	2	Inhibition of CYP26A1-mediated ATRA metabolism in human HL60 cells assessed as ATRA level at 5 uM incubated for 72 hrs by HPLC method (Rvb = 3.6 uM)	26365710
CHEMBL3620665	2	Inhibition of CYP26A1-mediated ATRA metabolism in human HL60 cells assessed as ATRA level at 5 uM incubated for 48 hrs by HPLC method (Rvb = 4.95 uM)	26365710
CHEMBL3620664	2	Inhibition of CYP26A1-mediated ATRA metabolism in human HL60 cells assessed as ATRA level at 5 uM incubated for 24 hrs by HPLC method (Rvb = 7.19 uM)	26365710
CHEMBL3620653	16	Inhibition of CYP26A1 in ATRA-induced human HL60 cell microsomes incubated for 30 mins in dark condition with NADPH and ATRA by HPLC method	26365710
CHEMBL3620652	4	Inhibition of CYP26A1 (unknown origin)	26365710
CHEMBL3399274	22	Inhibition of CYP26A1 in ATRA-induced human HL60 cell microsomes incubated for 30 mins using ATRA and NADPH by HPLC method	25684424
CHEMBL2417110	2	Inhibition of CYP26A1 in human NB4 cells assessed as ATRA level in medium at 5 uM after 12 hrs by LC-MS/MS analysis (Rvb = 27.05 +/- 1.34 ng/ml)	23601821
CHEMBL2214483	9	Inhibition of CYP26A1 in human MCF7 cell microsomes using [3H]ATRA as substrate after 1 hr by scintillation counter analysis	22727372
CHEMBL2148657	16	Inhibition of CYP26A1-mediated retinoic acid metabolism in human MCF7 cell microsomes using [3H]ATRA as substrate after 1 hr by scintillation counting	22989911
CHEMBL1833546	3	Inhibition of CYP26 in human liver microsomes	21838328
CHEMBL1833279	18	Inhibition of human CYP26A1 assessed using [11,12-3H]ATRA as substrate by scintillation counting	21838328
CHEMBL1768149	18	Inhibition of CYP26A1 in human MCF7 cell microsomes using [3H]ATRA after 1 hr by scintillation counting	21428449
CHEMBL996935	15	Inhibition of CYP26A1 in human MCF7 cells	18722776
CHEMBL926263	1	Inhibition of CYP26	17544277
CHEMBL916381	1	Inhibition of ATRA-induced CYP26 in human T47D cells assessed as ATRA metabolism using [11.12-3H]-ATRA up to 10 uM	15615521
CHEMBL916380	1	Inhibition of ATRA-induced CYP26 in human MCF7 cells assessed as ATRA metabolism using [11.12-3H]-ATRA up to 10 uM	15615521
CHEMBL916379	19	Inhibition of ATRA-induced CYP26 in human T47D cell microsome assessed as ATRA metabolism using [11.12-3H]-ATRA	15615521
CHEMBL916378	18	Inhibition of ATRA-induced CYP26 in human T47D cells assessed as ATRA metabolism using [11.12-3H]-ATRA	15615521
CHEMBL916377	18	Inhibition of ATRA-induced CYP26 in human MCF7 cells assessed ATRA as metabolism using [11.12-3H]-ATRA	15615521
CHEMBL853200	20	Inhibition of CYP26 expressed in human T47D cell line	16504501
CHEMBL865876	6	Activity against CYP26 up to 20 uM	16451067
CHEMBL832851	31	Potency towards cytochrome P 450 26 enzyme activity	15745819
CHEMBL3789263	24	Inhibition of microsomal fraction of human CYP26B1 expressed in Sf9 cells using 9-cis-RA as substrate preincubated for 5 mins followed by NADPH addition measured after 5 mins by HPLC analysis in presence of rat P450 reductase	26918322
CHEMBL3789262	1	Inhibition of microsomal fraction of human CYP26B1 expressed in Sf9 cells using 9-cis-RA as substrate at 20 uM preincubated for 5 mins followed by NADPH addition measured after 5 mins by HPLC analysis in presence of rat P450 reductase	26918322

Tab. S8: Summary of ChEMBL records returned by a search on "retinol dehydrogenase"

Assay ID	Chem Ct	Assay description	PMID
CHEMBL4260594	1	Inhibition of ADH1B (unknown origin) assessed as reduction in NADH production by spectrophotometric analysis	30340896
CHEMBL641134	23	Inhibition of human alcohol dehydrogenase beta 1 activity	9572895
CHEMBL641140	1	Inhibitory activity against human alcohol dehydrogenase sigma.	9572895
CHEMBL641139	3	Inhibitory activity against human alcohol dehydrogenase sigma; ND=not determined	9572895
CHEMBL641138	19	Inhibition of human alcohol dehydrogenase sigma activity	9572895
CHEMBL641137	4	Inhibitory activity against human alcohol dehydrogenase pi; ND=not determined	9572895
CHEMBL641136	19	Inhibition of human alcohol dehydrogenase pi activity	9572895

CHEMBL1031472	8	Inhibition of 3alpha-HSD	19188072
CHEMBL892201	3	Inhibition of 3alphaHSD	17346963
CHEMBL898185	2	Inhibition of rat liver 3-alpha-HSD assessed as 5-beta-dihydrocortisone reduction at 500 uM	17517512
CHEMBL898184	2	Inhibition of rat liver 3alphaHSD assessed as 5-beta-dihydrocortisone reduction at 250 uM	17517512
CHEMBL898183	21	Inhibition of rat liver 3-alpha-HSD assessed as 5-beta-dihydrocortisone reduction	17517512
CHEMBL898182	17	Inhibition of rat liver 3alphaHSD assessed as 5-beta-dihydrocortisone reduction at 1 mM	17517512
CHEMBL3282425	2	Binding affinity to alcohol dehydrogenase (unknown origin)	1246029
CHEMBL3257323	5	Inhibition of alcohol dehydrogenase (unknown origin) assessed as dissociation constant for the complex of enzyme and DPNH	321782
CHEMBL822089	1	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the presence of 1 mM NAD+k	7009869
CHEMBL822088	1	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the absence of NAD+K	7009869
CHEMBL645349	7	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the presence of 1 mM NAD+k	7009869
CHEMBL875754	1	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the presence of 1 mM NAD+K	7009869
CHEMBL645348	1	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the presence of 1 mM NAD+(K	7009869
CHEMBL645347	10	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the absence of NAD+K	7009869
CHEMBL645346	1	The compound was tested for the ability to inactivate human liver alcohol dehydrogenase in the absence of NAD+(K	7009869
CHEMBL876583	1	Michaelis-Menten's constant was determined in vitro against purified rat liver alcohol dehydrogenase in presence of ethanol	6343601
CHEMBL645231	5	In vitro inhibitory constant against monkey liver alcohol dehydrogenase was determined	3155552

Tab. S9: Summary of Protein Data Bank records for Aldehyde Dehydrogenase (ALDH1A1, ALDH1A2, ALDH1A3)

PDB ID	Structure title	PMID	Year Dep	Ligands used
4WB9	Human ALDH1A1 complexed with NADH	25450233	2014	1,4-DIHYDRONICOTINAMIDE ADENINE DINUCLEOTIDE / CHLORIDE ION / YTTERBIUM (III) ION
4WJ9	Structure of Human apo ALDH1A1	25450233	2014	CHLORIDE ION / YTTERBIUM (III) ION
4WP7	Structure of human ALDH1A1 with inhibitor CM026	25634381	2014	8-{[4-(furan-2-ylcarbonyl)piperazin-1-yl]methyl}-1,3-dimethyl-7-(3-methylbutyl)-3,7-dihydro-1H-purine-2,6-dione / CHLORIDE ION / YTTERBIUM (III) ION
4WPN	Structure of human ALDH1A1 with inhibitor CM053	25634381	2014	1-{[1,3-dimethyl-7-(3-methylbutyl)-2,6-dioxo-2,3,6,7-tetrahydro-1H-purin-8-yl]methyl}piperidine-4-carboxamide / CHLORIDE ION / YTTERBIUM (III) ION
4X4L	Structure of human ALDH1A1 with inhibitor CM037	25634381	2014	1,4-DIHYDRONICOTINAMIDE ADENINE DINUCLEOTIDE / CHLORIDE ION / ethyl ({4-oxo-3-[3-(pyrrolidin-1-yl)propyl]-3,4-dihydro[1]benzothieno[3,2-d]pyrimidin-2-yl}sulfanyl)acetate / SODIUM ION / YTTERBIUM (III) ION
5FHZ	Human aldehyde dehydrogenase 1A3 complexed with NAD(+) and retinoic acid	27759097	2015	NICOTINAMIDE-ADENINE-DINUCLEOTIDE / RETINOIC ACID
5L2M	Structure of ALDH1A1 in complex with BUC11	28219011	2016	2,3,5-trimethyl-6-[3-oxo-3-(piperidin-1-yl)propyl]-7H-furo[3,2-g][1]benzopyran-7-one / CHLORIDE ION / S-HYDROXYCYSTEINE / YTTERBIUM (III) ION
5L2N	Structure of ALDH1A1 in complex with BUC25	28219011	2016	3-benzyl-4-methyl-2-oxo-2H-1-benzopyran-7-yl methanesulfonate / CHLORIDE ION / S-HYDROXYCYSTEINE / YTTERBIUM (III) ION
5L2O	Crystal Structure of ALDH1A1 in complex with BUC22	28219011	2016	7-(diethylamino)-4-methyl-2H-1-benzopyran-2-one / CHLORIDE ION / YTTERBIUM (III) ION
5TEI	Structure of human ALDH1A1 with inhibitor CM039	N/A	2016	1,4-DIHYDRONICOTINAMIDE ADENINE DINUCLEOTIDE / 6-{[(3-

				fluorophenyl)methyl]sulfanyl}-5-(2-methylphenyl)-2,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one / CHLORIDE ION / YTTERBIUM (III) ION
6DUM	ALDH1A1 N121S in complex with 6-{[(3-fluorophenyl)methyl]sulfanyl}-2-(oxetan-3-yl)-5-phenyl-2,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one (compound 13g)	30221940	2018	1,4-DIHYDRONICOTINAMIDE ADENINE DINUCLEOTIDE / 6-{[(3-fluorophenyl)methyl]sulfanyl}-2-(oxetan-3-yl)-5-phenyl-2,5-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one / CHLORIDE ION / YTTERBIUM (III) ION
5FHZ	Human aldehyde dehydrogenase 1A3 complexed with NAD(+) and retinoic acid	27759097	2015	NICOTINAMIDE-ADENINE-DINUCLEOTIDE / RETINOIC ACID
4X2Q	Crystal Structure of Human Aldehyde Dehydrogenase, ALDH1a2	N/A	2014	NICOTINAMIDE-ADENINE-DINUCLEOTIDE
6ALJ	ALDH1A2 liganded with NAD and compound WIN18,446	29240402	2017	N,N'-(octane-1,8-diyl)bis(2,2-dichloroacetamide)/NICOTINAMIDE-ADENINE-DINUCLEOTIDE
6B5G	ALDH1A2 liganded with NAD and (3-ethoxythiophen-2-yl){4-[4-nitro-3-(pyrrolidin-1-yl)phenyl]piperazin-1-yl}methanone (compound 6-118)	29240402	2017	(3-ethoxythiophen-2-yl){4-[4-nitro-3-(pyrrolidin-1-yl)phenyl]piperazin-1-yl}methanone / NICOTINAMIDE-ADENINE-DINUCLEOTIDE
6B5H	ALDH1A2 liganded with NAD and 1-(4-cyanophenyl)-N-(3-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1H-pyrazole-4-carboxamide (compound CM121)	29240402	2017	1-(4-cyanophenyl)-N-(3-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1H-pyrazole-4-carboxamide / NICOTINAMIDE-ADENINE-DINUCLEOTIDE
6B5I	ALDH1A2 liganded with 1-(4-cyanophenyl)-N-(3-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1H-pyrazole-4-carboxamide (compound CM121)	29240402	2017	1-(4-cyanophenyl)-N-(3-fluorophenyl)-3-[4-(methylsulfonyl)phenyl]-1H-pyrazole-4-carboxamide

Tab. S10: Summary of ChEMBL results for Aldehyde Dehydrogenase (ALDH1A1, ALDH1A2, ALDH1A3)

Assay ID	Chem Ct	Assay Description	PMID
CHEMBL4009360	1	Non-competitive inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level using varying levels acetaldehyde in presence of NAD+ by Lineweaver-Burk plot analysis	28219011
CHEMBL4009355	2	Non-competitive inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level using varying levels propionaldehyde in presence of NAD+ by Lineweaver-Burk plot analysis	28219011
CHEMBL4009350	1	Uncompetitive inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) using propionaldehyde as substrate in presence of varying levels NAD+ by Lineweaver-Burk plot analysis	28219011
CHEMBL4009344	37	Inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) assessed as remaining dehydrogenase activity by measuring NAD(P)H level at 10 uM preincubated for 2 mins followed by addition of propionaldehyde as substrate in presence of NAD+ by spectrophotometric method	28219011
CHEMBL4009338	3	Inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level preincubated for 2 mins followed by addition of propionaldehyde as substrate in presence of NAD+ by spectrophotometric method relative to control	28219011
CHEMBL4009337	15	Inhibition of full length recombinant human ALDH1A1 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level preincubated for 2 mins followed by addition of propionaldehyde as substrate in presence of NAD+ by spectrophotometric method	28219011
CHEMBL3888331	16	Inhibition Assay: IC50 values were determined for CB29 and its analogs using propionaldehyde as the substrate for ALDH1A1 and ALDH2 or benzaldehyde as the substrate for ALDH3A1.	N/A
CHEMBL3562125	231	PubChem BioAssay. Extended Characterization of HPGD Inhibitors: Counterscreen Against ALDH1A1. (Class of assay: confirmatory)	N/A
CHEMBL3419577	1	Non-competitive partial inhibition of recombinant human ALDH1A1 using 800 uM NAD+ as cofactor by Lineweaver-Burk plot analysis in presence of 100 to 800 uM acetaldehyde	25634381
CHEMBL3419576	20	Inhibition of recombinant human ALDH1A1 using propionaldehyde as substrate preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3418217	1	Inhibition of recombinant human ALDH1A1 using propionaldehyde as substrate at 20 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381

CHEMBL3418216	2	Inhibition of human ALDH1A1 G458N mutant using propionaldehyde as substrate preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3418011	1	Inhibition of human ALDH1A1 G458N mutant using propionaldehyde as substrate at 20 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3418010	17	Inhibition of human ALDH1A1 G458N mutant using propionaldehyde as substrate at 100 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis relative to control	25634381
CHEMBL3418009	1	Competitive tight inhibition of recombinant human ALDH1A1 using 1000 uM NAD+ as cofactor by Lineweaver-Burk plot analysis in presence of 100 to 800 uM acetaldehyde	25634381
CHEMBL3418008	1	Non-competitive tight inhibition of recombinant human ALDH1A1 using 1000 uM NAD+ as cofactor by Lineweaver-Burk plot analysis in presence of 100 to 800 uM acetaldehyde	25634381
CHEMBL3418007	2	Effect on recombinant human ALDH1A1 using propionaldehyde as substrate up to 250 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3421198	1	Uncompetitive partial inhibition of recombinant human ALDH1A1 using 200 uM propionaldehyde as substrate by Lineweaver-Burk plot analysis in presence of 25 to 250 uM NAD+	25634381
CHEMBL3421186	5	Inhibition of recombinant human ALDH1A1 using propionaldehyde as substrate at 100 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis relative to control	25634381
CHEMBL3421185	1	Competitive inhibition of recombinant human ALDH1A1 using 800 uM NAD+ as cofactor by Lineweaver-Burk plot analysis in presence of 100 to 800 uM acetaldehyde	25634381
CHEMBL3130567	22	Inhibition of human ALDH1A1 using propionaldehyde as substrate preincubated for 2 mins followed by substrate addition by spectrophotometry in presence of NAD+	24444054
CHEMBL3130566	1	Noncompetitive/mixed type inhibition of human ALDH1A1 by Lineweaver-Burk plot analysis in presence of NAD+	24444054
CHEMBL3128579	1	Competitive inhibition of human ALDH1A1 using propionaldehyde as substrate by Lineweaver-Burk plot analysis	24444054
CHEMBL3118330	1	Inhibition of human ALDH1A1 using propionaldehyde as substrate up to 250 uM preincubated for 1 min followed by substrate addition by spectrophotometric analysis	24387105
CHEMBL3118132	21	Inhibition of human ALDH1A1 using propionaldehyde as substrate preincubated for 1 min followed by substrate addition by spectrophotometric analysis	24387105
CHEMBL3118130	3	Activation of human ALDH1A1 using propionaldehyde as substrate at 100 uM preincubated for 1 min followed by substrate addition by spectrophotometric analysis	24387105
CHEMBL3107142	9	Inhibition of ALDH1A1 (unknown origin) using NAD+/propionaldehyde as substrate after 15 mins by UV-fluorescence assay	24360556
CHEMBL1738585	87	PUBCHEM_BIOASSAY: Inhibitors of Aldehyde Dehydrogenase 1 (ALDH1A1): Follow up Confirmation and Counterscreen. (Class of assay: confirmatory) [Related pubchem assays (depositor defined):AID1030, AID2407]	N/A
CHEMBL1614458	16117	PUBCHEM_BIOASSAY: qHTS Assay for Inhibitors of Aldehyde Dehydrogenase 1 (ALDH1A1). (Class of assay: confirmatory) [Related pubchem assays: 1030 (qHTS Validation Assay for Inhibitors of aldehyde dehydrogenase 1 (ALDH1A1))]	N/A
CHEMBL1110890	6	Inhibition of ALDH1 in human K562 cells at 15 uM after 45 mins by flow cytometry based method relative to bodipy-aminoacetaldehyde	20222671
CHEMBL1019415	1	Effect on human recombinant his-tagged cytosolic ALDH1A1 activity expressed in Escherichia coli BL21 cells at 100 uM	18787169
CHEMBL997777	1	Inhibition of ALDH1	17692435
CHEMBL997770	2	Inhibition of ALDH1 in human DU145 cells at 7.5 uM after 3 days	17692435
CHEMBL997769	2	Inhibition of ALDH1 in human DU145 cells at 5 uM after 3 days	17692435
CHEMBL997768	2	Inhibition of ALDH1 in human DU145 cells at 2.5 uM after 3 days	17692435
CHEMBL844222	1	Inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are treated with phenobarbital (PB)	7392033
CHEMBL643983	12	Inhibitory activity against yeast aldehyde dehydrogenase (AIDH)	9667978
CHEMBL643982	3	Inhibitory activity against aldehyde dehydrogenase in rats.	9191964
CHEMBL643981	1	Evaluated for inhibition of hepatic mitochondrial Aldehyde dehydrogenase (ALDH) from rat	7990120
CHEMBL641149	1	Evaluated for inhibition of class II mitochondrial Aldehyde dehydrogenase (ALDH) in osmotically disrupted mitochondria from rat	7990120
CHEMBL875244	3	Evaluated in vivo for inhibition of liver mitochondrial aldehyde dehydrogenase activity 2 hour after administering into 5 to 8 rats, and percentage of activity remaining was reported at a concentration of 1.25 mmol/Kg	6541256

CHEMBL641148	2	Evaluated in vivo for inhibition of liver mitochondrial aldehyde dehydrogenase activity 2 hour after administering into rats, at a dose of 1.25 mmol/kg	6541256
CHEMBL641147	1	Evaluated in vivo for inhibition of liver mitochondrial aldehyde dehydrogenase activity 2 hour after administering into 5 to 8 rats, at a dose of 1.25 mmol/kg	6541256
CHEMBL641146	7	Evaluated in vitro for inhibition of mitochondrial aldehyde dehydrogenase activity in intact rat liver mitochondria (1.0 mM)	6541256
CHEMBL641145	4	Evaluated in vitro for inhibition of mitochondrial aldehyde dehydrogenase activity in disrupted rat liver mitochondria (1.0 mM)	6541256
CHEMBL641144	9	Evaluated in vitro for inhibition of mitochondrial aldehyde dehydrogenase (AIDH) activity in intact rat liver mitochondria (0.2 mM)	6541256
CHEMBL641143	5	Evaluated in vitro for inhibition of mitochondrial aldehyde dehydrogenase (AIDH) activity in disrupted rat liver mitochondria (0.2 mM)	6541256
CHEMBL646632	2	Compound was tested for enantioselectivity of alcohol dehydrogenase in yeast at a concentration of 100 ug/mL.	9871718
CHEMBL646624	2	Inhibitory activity against yeast alcohol dehydrogenase	1433175
CHEMBL646623	1	In vitro inhibitory activity against yeast Alcohol dehydrogenase	10514271
CHEMBL646622	1	In vitro inhibition against yeast Alcohol dehydrogenase; IA means In active	7783119
CHEMBL646621	7	In vitro inhibition against yeast Alcohol dehydrogenase	7783119
CHEMBL646620	3	In vitro inhibition against yeast Alcohol dehydrogenase	7783118
CHEMBL646619	2	In vitro inhibitory activity against yeast alcohol dehydrogenase; Active	1433175
CHEMBL646616	1	Percent inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are treated with phenobarbital (PB)	7392033
CHEMBL646615	1	Percent inhibition of rat hepatic mitochondrial Alcohol dehydrogenase	10514271
CHEMBL646614	5	Percent inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are untreated with phenobarbital (PB)	7392033
CHEMBL646613	4	Percent inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are treated with phenobarbital (PB)	7392033
CHEMBL646612	6	Inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are untreated with phenobarbital (PB)	7392033
CHEMBL646611	4	Inhibition of the enzyme Alcohol dehydrogenase was measured in rats which are treated with phenobarbital (PB)	7392033
CHEMBL645356	4	Inhibitory activity against porcine alcohol dehydrogenase; Active	1433175
CHEMBL645232	2	Compound was tested for enantioselectivity of alcohol dehydrogenase in thermoanaerobium brockii at a concentration of 5 ug/mL.	9871718
CHEMBL645230	2	Compound was tested for enantioselectivity of alcohol dehydrogenase in lactobacillus kefir at a concentration of 50 ug/mL.	9871718
CHEMBL4009340	1	Inhibition of full length recombinant human ALDH1A2 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level preincubated for 2 mins followed by addition of propionaldehyde as substrate in presence of NAD+ by spectrophotometric method relative to control	28219011
CHEMBL4009339	12	Inhibition of full length recombinant human ALDH1A2 expressed in Escherichia coli BL21(DE3) assessed as reduction in dehydrogenase activity by measuring NAD(P)H level preincubated for 2 mins followed by addition of propionaldehyde as substrate in presence of NAD+ by spectrophotometric method	28219011
CHEMBL3419574	12	Inhibition of recombinant human ALDH1A2 using propionaldehyde as substrate at 100 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3419565	1	Effect on recombinant human ALDH1A2 using propionaldehyde as substrate at 20 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3418002	17	Activation of recombinant human ALDH1A2 using propionaldehyde as substrate at 20 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3421188	3	Activation of recombinant human ALDH1A2 using propionaldehyde as substrate at 100 uM preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3421187	4	Inhibition of recombinant human ALDH1A2 using propionaldehyde as substrate preincubated for 2 mins with NAD+ followed by substrate addition by UV-Vis spectrophotometric analysis	25634381
CHEMBL3118138	1	Inhibition of human ALDH1A2 using propionaldehyde as substrate up to 250 uM preincubated for 1 min followed by substrate addition by spectrophotometric analysis	24387105
CHEMBL3118129	24	Inhibition of human ALDH1A2 using propionaldehyde as substrate up to 100 uM preincubated for 1 min followed by substrate addition by spectrophotometric analysis	24387105

Tab. S11: Summary of Protein Data Bank entries for Retinoic acid receptor alpha (RARa)

PDB ID	Structure title	PMID	Year Dep	Ligands used
1DKF	CRYSTAL STRUCTURE OF A HETERODIMERIC COMPLEX OF RAR AND RXR LIGAND-BINDING DOMAINS	10882070	1999	4-[(4,4-DIMETHYL-1,2,3,4-TETRAHYDRO-[1,2']BINAPTHALENYL-7-CARBONYL)-AMINO]-BENZOIC ACID / OLEIC ACID
1DSZ	STRUCTURE OF THE RXR/RAR DNA-BINDING DOMAIN HETERODIMER IN COMPLEX WITH THE RETINOIC ACID RESPONSE ELEMENT DR1	10698945	2000	ZINC ION
3A9E	Crystal structure of a mixed agonist-bound RAR-alpha and antagonist-bound RXR-alpha heterodimer ligand binding domains	21152046	2009	(2E,4E,6Z)-3-methyl-7-(5,5,8,8-tetramethyl-3-propoxy-5,6,7,8-tetrahydronaphthalen-2-yl)octa-2,4,6-trienoic acid / RETINOIC ACID
3KMR	Crystal structure of RARalpha ligand binding domain in complex with an agonist ligand (Am580) and a coactivator fragment	20543827	2009	4-{[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)carbonyl]amino}benzoic acid
3KMZ	Crystal structure of RARalpha ligand binding domain in complex with the inverse agonist BMS493 and a corepressor fragment	20543827	2009	4-{(E)-2-[5,5-dimethyl-8-(phenylethynyl)-5,6-dihydronaphthalen-2-yl]ethenyl}benzoic acid / GLYCEROL / S-HYDROXYCYSTEINE
4DQM	Revealing a marine natural product as a novel agonist for retinoic acid receptors with a unique binding mode and antitumor activity	22642567	2012	(5S)-4-[(3E,7E)-4,8-dimethyl-10-(2,6,6-trimethylcyclohex-1-en-1-yl)deca-3,7-dien-1-yl]-5-hydroxyfuran-2(5H)-one
5K13	Crystal structure of the RAR alpha ligand-binding domain in complex with an antagonist	27261179	2016	4-{5-(3-tert-butylphenyl)-1-[4-(methylsulfonyl)phenyl]-1H-pyrazol-3-yl}benzoic acid

Tab. S12: Summary of ChEMBL results for Retinoic acid receptor alpha (RARa)

Assay ID	Chem Ct	Assay description	PMID
CHEMBL3880815	18	Activation of RARalpha (unknown origin) expressed in human HeLa cells co-expressing ERE-beta-Glob-Luc-SV-Neo incubated for 18 hrs by luciferase reporter gene assay	N/A
CHEMBL3224186	6	Inhibition of RAR alpha (unknown origin)	N/A
CHEMBL799803	9	Binding affinity towards Retinoic acid receptor alpha	N/A
CHEMBL799801	10	Inhibition of [3H]ATRA binding to retinoic acid receptor RAR alpha	N/A
CHEMBL799715	10	Percent efficacy for retinoic acid receptor RAR alpha in CV-1 cell transcriptional activation assay	N/A
CHEMBL799710	10	Effective potency in transcriptional activation assay in CV-1 cells expressing retinoic acid receptor RAR alpha; Not active	N/A
CHEMBL799700	5	Agonist activity for retinoic acid receptor RAR alpha in transcriptional activation assay; NA means not active (EC50>10e4 nM)	N/A
CHEMBL799699	6	Agonist activity for retinoic acid receptor RAR alpha in transcriptional activation assay	N/A
CHEMBL799686	25	Maximum retinoic acid receptor (RAR)-alpha transactivation activity relative to retinoic acid at 10e-6 M	N/A
CHEMBL799685	2	Transcriptional activation activity against retinoic acid receptor RAR alpha; Not active	N/A
CHEMBL799684	10	Transcriptional activation activity against retinoic acid receptor RAR alpha; Not active	N/A
CHEMBL799683	13	Transcriptional activation activity against retinoic acid receptor RAR alpha	N/A
CHEMBL798143	1	Binding affinity for Retinoic acid receptor alpha	N/A
CHEMBL798141	1	Transactivation potency for Retinoic acid receptor alpha	N/A
CHEMBL802573	6	Inhibition of [3H]ATRA binding to RAR alpha receptor	N/A
CHEMBL799721	7	Compound was tested for binding affinity against retinoic acid receptor using 5 nM of [3H]RA as a radioligand in baculovirus expressed receptor	N/A
CHEMBL799717	1	Binding affinity for Retinoic acid receptor alpha; Not active	N/A
CHEMBL799876	9	Binding affinity for Retinoic acid receptor alpha	N/A
CHEMBL799865	6	Maximal transcriptional activation in CV-1 cells expressing RAR alpha receptor relative to ATRA	N/A
CHEMBL799863	8	Transactivation potency for Retinoic acid receptor alpha; Not active	N/A
CHEMBL879144	2	Transactivation potency for Retinoic acid receptor alpha	N/A
CHEMBL799859	7	Compound was tested for functional activity in CV-1 cells transfected with an expression vector for retinoic acid receptor alpha using transactivation assay	N/A
CHEMBL799858	5	Transcriptional activation in CV-1 cells expressing retinoic acid receptor RAR	N/A

		alpha; not active	
CHEMBL799857	1	Transcriptional activation in CV-1 cells expressing retinoic acid receptor RAR alpha; inactive	N/A
CHEMBL802230	4	Transcriptional activation of retinoic acid receptor RAR alpha; not active	N/A
CHEMBL802229	4	Transcriptional activation of retinoic acid receptor RAR alpha	N/A
CHEMBL799977	3	Binding affinity towards human Retinoic acid receptor alpha	N/A
CHEMBL772400	13	Maximal transcriptional activation of RAR-alpha relative to retinoic acid at 10e-6 M	N/A
CHEMBL772399	8	Transcriptional activation of retinoic acid RAR-alpha receptor; Not active	N/A
CHEMBL772398	5	Transcriptional activation of retinoic acid RAR-alpha receptor	N/A
CHEMBL772309	2	Transcriptional activation for RAR alpha receptor; not active (EC50>10e4 nM)	N/A
CHEMBL772308	9	Transcriptional activation for RAR alpha receptor	N/A
CHEMBL799712	1	Transcriptional activation in CV-1 cells expressing RAR-alpha receptor; Not active	9733501
CHEMBL799711	9	Transcriptional activation in CV-1 cells expressing RAR-alpha receptor	9733501
CHEMBL799790	2	Percent maximal induction of human RAR-alpha receptor relative to ATRA; Inactive	9703470
CHEMBL799789	1	Percent maximal induction of human RAR-alpha receptor relative to ATRA; Inactive	9703470
CHEMBL799716	3	Percent maximal induction of human RAR-alpha receptor relative to ATRA	9703470
CHEMBL801810	1	Relative IC50 for human RAR-alpha receptor as IC50(compound) divided by IC50(ATRA)	9703470
CHEMBL801809	2	Relative IC50 for human RAR-alpha receptor as IC50(compound) divided by IC50(ATRA)	9703470
CHEMBL801808	1	Relative EC30 for human RAR-alpha receptor as EC30(compound) divided by EC30(ATRA); Not detected at 500 nM	9703470
CHEMBL801807	1	Relative EC30 for human RAR-alpha receptor as EC30(compound) divided by EC30(ATRA); Inactive	9703470
CHEMBL801806	1	Relative EC30 for human RAR-alpha receptor as EC30(compound) divided by EC30(ATRA); Inactive	9703470
CHEMBL799987	5	Relative EC30 for human RAR-alpha receptor as EC30(compound) divided by EC30(ATRA)	9703470
CHEMBL802719	8	Inhibition of binding to retinoid A receptor RAR alpha	9572893
CHEMBL801816	1	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR alpha	9572893
CHEMBL801815	7	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR alpha	9572893
CHEMBL799805	4	Synergistic activity towards retinoic acid receptor-alpha	9435893
CHEMBL799804	1	Selective activity towards retinoic acid receptor-alpha	9435893
CHEMBL799798	2	Antagonistic activity towards retinoic acid receptor-alpha	9435893
CHEMBL873431	2	Agonistic activity towards retinoic acid receptor-alpha	9435893
CHEMBL799795	6	Inhibition of [3H]ATRA binding to baculovirus expressed RAR alpha receptor	9258350
CHEMBL857604	4	Inhibition of [3H]ATRA binding to baculovirus expressed Retinoic acid receptor RAR alpha	8978832
CHEMBL799861	1	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor RAR alpha	8978832
CHEMBL802722	10	Percent inhibition of [3H]ATRA binding to mouse Retinoic acid receptor RAR alpha	8809153
CHEMBL801817	10	Inhibition of [3H]ATRA binding to mouse Retinoic acid receptor RAR alpha	8809153
CHEMBL801814	6	Transcriptional activation of Retinoic acid receptor RAR alpha;NA=not active	8784454
CHEMBL801813	2	Transcriptional activation of Retinoic acid receptor RAR alpha	8784454
CHEMBL802721	1	Dissociation constant for binding to Retinoic acid receptor alpha;NA=not active	8784454
CHEMBL802720	7	Dissociation constant for binding to Retinoic acid receptor alpha	8784454
CHEMBL799799	3	Inhibition of [3H]ATRA binding to Retinoic acid receptor RAR alpha	8765503
CHEMBL799702	3	Transcriptional activation of Retinoic acid receptor RAR alpha	8765503
CHEMBL799875	5	Binding affinity for baculovirus-expressed Retinoic acid receptor RAR alpha	8759622
CHEMBL877734	4	Inhibition of [3H]ATRA binding to Retinoic acid receptor RAR alpha	8709094
CHEMBL799866	4	Percent transcriptional activation relative to ATRA in CV-1 cells expressing Retinoic acid receptor RAR alpha	8709094
CHEMBL884092	4	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor RAR alpha	8709094
CHEMBL799794	11	Apparent binding constant against Retinoic acid receptor alpha in HeLa cell GAl-4 transactivation assay	8691435

CHEMBL799802	25	Binding affinity to retinoic acid receptor alpha using [3H]CD 367 as radioligand	8544175
CHEMBL884081	11	Effective concentration against RAR-alpha receptor	8410972
CHEMBL772397	17	Retinoid activity at 10 e-5 M (E)-RA against RAR-alpha receptor for gene transcriptional activation in transfected CV-1 cells	8410972
CHEMBL772396	1	Effective concentration against RAR-alpha receptor	8410972
CHEMBL799871	6	Binding affinity against retinoic Acid alpha receptor using [3H]- -9-cis-Retinoic Acid in competitive binding assay	8308867
CHEMBL798386	6	Binding affinity against retinoic Acid alpha receptors co-transfected into CV-1 cells	8308867
CHEMBL799797	19	Inhibition of [3H]-ATRA binding to baculovirus expressed retinoid receptor RAR alpha	8071941
CHEMBL799705	20	Effective concentration against retinoid receptor isoform (RAR alpha) expressed in CV-1 cells	8071941
CHEMBL799618	1	Inhibition of [3H]ATRA binding to baculovirus expressed retinoid receptor RAR alpha	8071941
CHEMBL1017445	2	Transactivation of RARalpha expressed in mammalian cells assessed as effect on palindromic thyroid hormone response element-driven transcriptional activation by luciferase reporter gene assay	7807131
CHEMBL799862	1	Relative activity against Retinoic acid receptor RAR alpha compared to ATRA	7650690
CHEMBL802725	24	Relative activity against Retinoic acid receptor alpha at 10e-6 M with respect to 10e-6 M of trans-RA	7650690
CHEMBL802724	1	Inhibition of [3H]CD 367 binding to Retinoic acid receptor RAR alpha	7650690
CHEMBL799701	10	Transcriptional activation of Retinoic acid receptor RAR alpha	7636843
CHEMBL802718	7	Inhibition of murine Retinoic acid receptor RAR alpha	7608895
CHEMBL799720	1	Binding constant for baculovirus-expressed Retinoic acid receptor RAR alpha	7490725
CHEMBL798387	1	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor RAR alpha	7490725
CHEMBL4037125	3	Agonist activity at RARaplha (unknown origin)	28850227
CHEMBL4019429	1	Transactivation of human GAL4-fused RARalpha ligand binding domain expressed in HEL293T cells at 10 uM after 12 to 14 hrs by dual-glo luciferase reporter gene assay	28845983
CHEMBL4040808	1	Antagonist activity at GAL4-tagged human RARalpha1 ligand binding domain (177 to 462 residues) expressed in HEK293T cells at 1 uM after 12 to 14 hrs by dual-glo luciferase reporter gene assay	28749691
CHEMBL4040793	1	Transactivation of GAL4-tagged human RARalpha1 ligand binding domain (177 to 462 residues) expressed in HEK293T cells at 1 uM after 12 to 14 hrs by dual-glo luciferase reporter gene assay	28749691
CHEMBL3817435	1	Antagonist activity at RARalpha-LBD (unknown origin) expressed in HEK-293 cells assessed as inhibition of ATRA induced Gal4/luciferase gene expression after 24 hrs	27261179
CHEMBL3817429	11	Displacement of [3H]-TTNPB from RARalpha/RXRalpha (unknown origin) expressed in baculovirus expression system by scintillation proximity assay	27261179
CHEMBL3789268	3	Activation of human RARalpha at 1 uM by luciferase reporter gene assay	26918322
CHEMBL3778102	1	Inhibition of human RARalpha	26819660
CHEMBL3599161	1	Agonist activity at Gal4 DNA binding domain-tagged human RARalpha ligand binding domain expressed in HEK293 cells assessed as activation of receptor-mediated transcriptional activity by luciferase reporter gene assay	26048806
CHEMBL3599039	1	Antagonist activity at Gal4 DNA binding domain-tagged human RARalpha ligand binding domain expressed in HEK293 cells assessed as inhibition of receptor-mediated transcriptional activity by luciferase reporter gene assay	26048806
CHEMBL3583847	1	Binding affinity to RARalpha (unknown origin) at 10 uM	26023814
CHEMBL3405117	1	Agonist activity at RARalpha (unknown origin) expressed in HEK293 cells assessed as transcriptional activation at 0.01 to 0.1 uM after 48 hrs by luciferase reporter gene assay	25838141
CHEMBL3405115	4	Agonist activity at RARalpha (unknown origin) expressed in HEK293 cells assessed as transcriptional activation after 48 hrs by luciferase reporter gene assay in presence of bexarotene	25838141
CHEMBL3405114	8	Agonist activity at RARalpha (unknown origin) expressed in HEK293 cells assessed as transcriptional activation after 48 hrs by luciferase reporter gene assay	25838141
CHEMBL3405113	5	Agonist activity at RARalpha (unknown origin) expressed in HEK293 cells assessed as transcriptional activation at 1 uM after 48 hrs by luciferase reporter gene assay	25838141
CHEMBL3385866	2	Agonist activity at human RARalpha expressed in HEK293 cells by luciferase reporter gene assay	25305688
CHEMBL3370745	1	Antagonist activity against RARalpha ligand binding domain (unknown origin) expressed in human MCF7 cells assessed as inhibition of ATRA-induced	25057340

		receptor transactivation at 10 uM after 18 hrs by luciferase reporter gene based mammalian one-hybrid assay	
CHEMBL3370749	1	Antagonist activity against RXRalpha/RARalpha ligand binding domain (unknown origin) expressed in human HEK293T cells assessed as inhibition of 9-cis-RA/T09-induced receptor transactivation at 2 and 10 uM after 18 hrs by luciferase reporter gene based mammalian one-hybrid assay	25057340
CHEMBL3368375	2	Activation of human RAR-alpha expressed in HEK293 cells coexpressing with tk-betaRE-Luc after 24 hrs by luciferase reporter gene assay	24959987
CHEMBL3295537	3	Antagonist activity at Gal4-fused mouse RAR-alpha transfected in human HeLa cells after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295530	3	Agonist activity at Gal4-fused mouse RAR-alpha transfected in human HeLa cells at 1 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295525	3	Agonist activity at Gal4-fused mouse RAR-alpha transfected in human HeLa cells after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3367188	1	Activity at RARalpha (unknown origin)	24831826
CHEMBL3297476	5	Agonist activity at Gal4-fused human RAR-alpha expressed in HEK293 cells assessed as receptor-mediated transcriptional activity at 1 uM treated 24 hrs after transfection measured 48 hrs post-transfection by dual luciferase reporter assay	24801499
CHEMBL3292973	5	Agonist activity at human RARalpha expressed in HEK293 cells assessed as transcriptional activation at 0.1 to 50 uM after 40 hrs by luciferase reporter gene assay	24799257
CHEMBL3292971	1	Agonist activity at human RARalpha expressed in HEK293 cells assessed as transcriptional activation at 1 to 100 uM after 40 hrs by luciferase reporter gene assay in presence of RAR antagonist LE135	24799257
CHEMBL3292970	1	Agonist activity at human RARalpha expressed in HEK293 cells assessed as transcriptional activation at 1 to 100 uM after 40 hrs by luciferase reporter gene assay	24799257
CHEMBL3118436	25	Agonist activity at Gal4-fused RARalpha (unknown origin) transfected in HEK293 cells assessed as induction of transcriptional activity at 4 uM after 6 hrs by luciferase/beta-galactosidase reporter gene assay relative to control	24457093
CHEMBL3118434	24	Antagonist activity at Gal4-fused RARalpha (unknown origin) transfected in HEK293 cells assessed as ATRA-induced transcriptional activity at 4 uM by luciferase/beta-galactosidase reporter gene assay relative to ATRA-treated control	24457093
CHEMBL3118432	3	Antagonist activity at Gal4-fused RARalpha (unknown origin) transfected in HEK293 cells assessed as inhibition of ATRA-induced transcriptional activity by luciferase/beta-galactosidase reporter gene assay	24457093
CHEMBL3118431	1	Inverse agonist activity at RARalpha (unknown origin)	24457093
CHEMBL3100731	3	Agonist activity at human RARalpha expressed in HEK293 cells assessed as transcriptional activation at 10'-6 M after 48 hrs by luciferase reporter gene assay	24359708
CHEMBL2389682	2	Antagonist activity at human RARalpha expressed in human HeLa cells assessed as inhibition of ATRA-induced RARE transactivation after 24 hrs by chloramphenicol acetyltransferase reporter gene assay	24040487
CHEMBL2389681	2	Antagonist activity at human RARalpha expressed in human HeLa cells assessed as inhibition of ATRA-induced RARE-chloramphenicol acetyltransferase reporter gene expression after 24 hrs by transactivation competition assay	24040487
CHEMBL2401373	36	Transactivation of Gal4-fused RARalpha (unknown origin) expressed in African green monkey COS1 cells at 100 nM by luciferase reporter gene assay relative to DMSO-treated control	23685180
CHEMBL2401367	1	Activation of RXRalpha (unknown origin) by CAT reporter gene assay	23685180
CHEMBL2379064	1	Antagonist activity at RARalpha in human MCF7 cells assessed as inhibition of ATRA-induced luciferase activity after 48 hrs by luciferase reporter gene assay	23474897
CHEMBL2379063	1	Antagonist activity at RARalpha in human MCF7 cells assessed as inhibition of ATRA-induced luciferase activity at 10 nM after 48 hrs by luciferase reporter gene assay	23474897
CHEMBL2379966	1	Antagonist activity at RARalpha in human MCF7 cells assessed as inhibition of ATRA-induced luciferase activity at 0.1 to 1 nM after 48 hrs by luciferase reporter gene assay	23474897
CHEMBL2341874	1	Transactivation of RARalpha (unknown origin) by luciferase reporter gene assay relative to Am80	23391145
CHEMBL2051205	1	Induction of RARalpha degradation	22658364
CHEMBL1961828	2	Effect on RARA(NR1B1) dependent reporter activity in HEK293 cells at 20 uM	22460951
CHEMBL2155741	1	Displacement of [3H]ATRA from RARalpha overexpressed in COS cell extract at 10 nM after 12 hrs by liquid scintillation counting	21684744
CHEMBL2155740	1	Inhibition of transactivation of RARalpha overexpressed in COS cells after 24 hrs by luciferase reporter gene assay in presence of ATRA	21684744

CHEMBL2155736	1	Displacement of [3H]ATRA from RARalpha overexpressed in COS cell extract after 12 hrs by liquid scintillation counting	21684744
CHEMBL1815811	2	Transcriptional activation of human RARalpha at 1 uM by (TREpal)2-tk-CAT reporter gene assay	21548569
CHEMBL1815808	2	Transcriptional activation of human RARalpha at 0.1 uM by luciferase reporter gene assay relative to control	21548569
CHEMBL1768345	2	Antagonist activity at mouse RARalpha expressed in COS-1 cells assessed as inhibition of Am80-induced transactivation by luciferase reporter gene assay	21459577
CHEMBL1679782	1	Antagonist activity at RARalpha by TR-FRET assay	21218783
CHEMBL1679776	2	Agonist activity at RARalpha by TR-FRET assay	21218783
CHEMBL1671298	6	Effect on human Gal4-fused RAR alpha at 10 uM by luciferase reporter gene assay	21142112
CHEMBL1274439	1	Agonist activity at RARalpha	20925433
CHEMBL1227766	4	Transactivation of RARalpha in human COS7 cells at 10 uM by luciferase reporter gene assay	20656484
CHEMBL1211362	3	Agonist activity at RARalpha-LBD expressed in HEK293 cells assessed as Gal4-DBD interaction by cellular mammalian one hybrid assay relative to retinoic acid	20638278
CHEMBL1211337	3	Agonist activity at RARalpha-LBD expressed in HEK293 cells assessed as Gal4-DBD interaction by cellular mammalian one hybrid assay	20638278
CHEMBL1062038	4	Agonist activity at human RARalpha expressed in human Caco-2 cells assessed as induction of RARE-mediated transcriptional activity at 100 nM after 24 hrs by luciferase reporter gene assay relative to all-trans retinoic acid	19791803
CHEMBL1061276	4	Agonist activity at human RARalpha expressed in human Caco-2 cells assessed as induction of RARE-mediated transcriptional activity at 1 uM after 24 hrs by luciferase reporter gene assay relative to all-trans retinoic acid	19791803
CHEMBL1063213	1	Displacement of radioligand from RARalpha receptor	19502054
CHEMBL1785658	7	Antagonist activity at yeast GAL4 fused mouse RARalpha ligand binding domain expressed in HeLa cells assessed as inhibition of TTNPB-induced receptor transactivation by luciferase reporter gene assay	19482478
CHEMBL1785654	5	Agonist activity at yeast GAL4 fused mouse RARalpha ligand binding domain expressed in HeLa cells assessed as receptor transactivation by luciferase reporter gene assay	19482478
CHEMBL1021936	8	Activity at RARalpha/RXRalpha ligand binding domain assessed as stabilization of RXR helix H12 by fluorescence anisotropy in presence of up to 10 uM coactivator peptide TIF-NR2	19408900
CHEMBL1021933	1	Activity at RARalpha/RXRalpha ligand binding domain assessed as stabilization of RXR helix H12 by fluorescence anisotropy in presence of 1 uM coactivator peptide TIF-NR2	19408900
CHEMBL1021932	7	Activity at RARalpha/RXRalpha ligand binding domain assessed as stabilization of RXR helix H12 by fluorescence anisotropy	19408900
CHEMBL1022116	10	Activity at RARalpha expressed in mouse NIH3T3 cells by R-SAT assay	19239230
CHEMBL1022115	1	Activity at RARalpha expressed in mouse NIH3T3 cells at <10 uM by R-SAT assay relative to Am-580	19239230
CHEMBL1022114	10	Activity at RARalpha expressed in mouse NIH3T3 cells by R-SAT assay relative to Am-580	19239230
CHEMBL1031896	1	Displacement of [3H]9cRA from RARalpha	19216008
CHEMBL1029369	7	Inhibition of transactivation activity of Gal4-LBD fused human RARalpha (156 to 454) transfected in atRA-stimulated african green monkey CV1 cells at 0.2 uM after 6 hrs by Dual-light chemiluminescent assay	19216008
CHEMBL1029368	4	Inhibition of transactivation activity of Gal4-LBD fused human RARalpha (156 to 454) transfected in atRA-stimulated african green monkey CV1 cells at 4 uM after 6 hrs by Dual-light chemiluminescent assay	19216008
CHEMBL1029365	8	Transactivation of Gal4-LBD fused human RARalpha (156 to 454) transfected in african green monkey CV1 cells assessed as luciferase activity at 2 uM after 6 hrs by Dual-light chemiluminescent assay	19216008
CHEMBL1011985	5	Activity at human RARalpha ligand binding domain expressed in COS7 cells co-transfected with Gal4-DBD assessed as transcriptional activation after 16 hrs by Gal4 response element-driven luciferase reporter gene assay relative to all-trans retinoic acid	19058965
CHEMBL1011984	10	Activity at human RARalpha ligand binding domain expressed in COS7 cells co-transfected with Gal4-DBD assessed as transcriptional activation after 16 hrs by Gal4 response element-driven luciferase reporter gene assay	19058965
CHEMBL1029015	5	Activity at human RARalpha ligand binding domain expressed in COS7 cells co-transfected with Gal4-DBD assessed as transcriptional activation at 10 uM after 16 hrs by Gal4 response element-driven luciferase reporter gene assay relative to all-trans retinoic acid	19058965
CHEMBL1015265	2	Increase in transcriptional activity of RARalpha ligand binding domain expressed in human Hep G2 cells co-transfected with Gal4-DBD by luciferase	19053776

		reporter gene assay	
CHEMBL1023990	8	Agonist activity at human RARalpha expressed in human HeLa cells assessed as relative luminescence units at >=10 uM by luciferase assay relative to control	18951029
CHEMBL970653	5	Antagonist activity at human RARalpha expressed in african green monkey CV1 cells assessed as all-trans-retinoic acid-stimulated Gal4 transactivation activity by luciferase reporter gene assay	18702457
CHEMBL970650	11	Activity at human RARalpha expressed in african green monkey CV1 cells assessed as enhanced Gal4 transactivation activity by luciferase reporter gene assay	18702457
CHEMBL954844	3	Increase in transcriptional activity of RARalpha receptor epressed in human HaCaT cells co-transfected with DR5-tk-CAT reporter plasmid assessed as beta-galactosidase activity by CAT-ELISA	18511283
CHEMBL868240	3	Activity at human recombinant RARalpha by transactivation of TK-MH100x4-LUC reporter gene in HEK293 cells at 10 uM	16617018
CHEMBL916388	7	Displacement of [11,12-3H]ARTA from RARalpha	15615521
CHEMBL834984	1	Antagonism of retinoic acid receptor alpha in ATRA treated CV-1 cells co-expressing CRBP-I-tk-CAT reporter at 10e-7 M	15317450
CHEMBL834860	1	Antagonism of retinoic acid receptor alpha in ATRA treated CV-1 cells co-expressing CRBP-I-tk-CAT reporter at 10e-6 M	15317450
CHEMBL834854	1	Antagonism of retinoic acid receptor alpha in ATRA treated CV-1 cells co-expressing CRBP-I-tk-CAT reporter; control assay without compound	15317450
CHEMBL834845	2	Antagonism of retinoic acid receptor alpha activity induced by retinoic acid at 10e-7 M	15317450
CHEMBL834844	2	Antagonism of retinoic acid receptor alpha activity induced by retinoic acid at 10e-6 M	15317450
CHEMBL831146	2	Antagonism of retinoic acid receptor alpha activity induced by retinoic acid at 10e-5 M	15317450
CHEMBL836045	8	Agonist activity for Retinoic acid receptor alpha as photons in presence and absence of ligand	15261282
CHEMBL798144	3	Displacement of [3H]9-cis-RA from Retinoic acid receptor alpha LBD	15214780
CHEMBL659140	2	Transcriptional activation in CV-1 cells expressing RAR alpha at 1E-6M	15214780
CHEMBL799800	17	Binding affinity for retinoic acid receptor alpha (RARalpha), using 9-cis-[3H]-retinoic acid	15056000
CHEMBL884539	1	Inhibitory concentration for lipogenesis induced by retinoic acid receptor alpha in C3H10T1/2 clone 8 fibroblast cells	15056000
CHEMBL799709	3	Effective concentration for lipogenesis induced by retinoic acid receptor alpha in C3H10T1/2 clone 8 fibroblast cells; Not determined	15056000
CHEMBL799708	13	Effective concentration for retinoic acid receptor alpha induced lipogenesis in C3H10T1/2 clone 8 fibroblast cells	15056000
CHEMBL799707	5	Effective concentration for Retinoic acid receptor alpha activity in CV-1 cells; Not determined	15056000
CHEMBL799706	12	Effective concentration for Retinoic acid receptor alpha activity in CV-1 cells	15056000
CHEMBL800465	1	Displacement of [3H]ATRA from retinoic acid receptor RAR alpha; NT denotes not tested	15006411
CHEMBL799936	18	Binding affinity against retinoic acid receptor alpha by [3H]ATRA displacement.	15006411
CHEMBL803374	1	Displacement of [3H]-ATRA from RAR alpha receptor expressed in CV-1 cells; Not tested	14592510
CHEMBL803373	16	Binding affinity against RAR alpha receptor using [3H]ATRA as radioligand in CV-1 cells	14592510
CHEMBL656174	17	Agonist synergy against RAR alpha was tested along with 3 nM TTNPB	14592510
CHEMBL799935	4	Inhibition of [3H]-retinoic acid binding to murine retinoic acid receptor RAR alpha; ND means not determined	12723955
CHEMBL799934	2	Inhibition of [3H]-retinoic acid binding to murine retinoic acid receptor RAR alpha; NA means not applicable	12723955
CHEMBL799933	8	Inhibition of [3H]-retinoic acid binding to murine retinoic acid receptor RAR alpha	12723955
CHEMBL799796	6	Inhibition of [3H]ATRA binding to human Retinoic acid receptor RAR alpha	12482435
CHEMBL799704	3	Transcriptional activation in CV-1 cells expressing human Retinoic acid receptor RAR alpha; Not active	12482435
CHEMBL799703	4	Transcriptional activation in CV-1 cells expressing human Retinoic acid receptor RAR alpha	12482435
CHEMBL806021	1	Inhibition of [3H]ATRA binding to human Retinoic acid receptor RAR alpha	12482435
CHEMBL644678	6	Percent transcriptional activation of RAR alpha compared to 1 mM ATRA	12372520
CHEMBL644526	1	Percent transcriptional activation of RAR alpha compared to 1 mM ATRA	12372520
CHEMBL644525	7	Effective concentration for retinoic acid receptor RAR alpha transcriptional activation	12372520

CHEMBL644524	7	Binding affinity fo retinoic acid receptor RAR alpha	12372520
CHEMBL724247	1	Topical irritation induced by RAR alpha-selective retinoid Am-580 in mice; ND denotes not determined.	12372520
CHEMBL724246	2	Topical irritation induced by RAR alpha-selective retinoid Am-580 in mice	12372520
CHEMBL772307	4	Inhibition of [3H]ATRA binding to baculovirus expressed retinoic acid receptor RAR-alpha	11428923
CHEMBL772306	2	Transcriptional activation in CV-1 cells expressing retinoic acid receptor RAR alpha	11428923
CHEMBL799986	3	Agonistic activity on Retinoic acid receptor alpha by transcriptional activation in COS-1 cells incubated at 10e-9 M	11392543
CHEMBL878612	3	Agonistic activity on Retinoic acid receptor alpha by transcriptional activation in COS-1 cells incubated at 10e-8 M	11392543
CHEMBL799985	3	Agonistic activity on Retinoic acid receptor alpha by transcriptional activation in COS-1 cells incubated at 10e-7 M	11392543
CHEMBL799984	2	Agonistic activity on Retinoic acid receptor alpha by transcriptional activation in COS-1 cells incubated at 10e-6 M	11392543
CHEMBL799983	2	Agonistic activity on Retinoic acid receptor alpha by transcriptional activation in COS-1 cells incubated at 10e-10 M	11392543
CHEMBL802578	6	In vitro binding affinity towards Retinoic acid receptor alpha evaluated relative to that of All-trans retinoic acids(Mean of ATRA IC50 = 0.66 nM)	11354380
CHEMBL802575	2	Retinoid activity at Retinoic acid receptor alpha was evaluated relative to that of All-trans retinoic acids(Mean of ATRA EC50 = 1.06 nM); Not detectable	11354380
CHEMBL802574	4	Retinoid activity at Retinoic acid receptor alpha was evaluated relative to that of All-trans retinoic acids(Mean of ATRA EC50 = 1.06 nM)	11354380
CHEMBL799870	1	Antagonistic activity was evaluated in terms of inhibition of Retinoic acid receptor alpha transactivation by ATRA (50 nM)	11354380
CHEMBL799719	9	Binding affinity towards retinoic acid receptor alpha was determined using [3H]ATRA (5 nM) as radioligand	11277515
CHEMBL799869	5	Antagonist activity of TTNPB (10 nM) function at retinoic acid receptor alpha	11277515
CHEMBL799867	5	Efficacy of TTNPB (10 nM) function at retinoic acid receptor alpha (10 uM)	11277515
CHEMBL798385	3	Ability to inhibit TTNPB-induced transactivation at retinoic acid receptor alpha	11277515
CHEMBL799982	1	Inhibition of [3H]ATRA binding to Retinoic acid receptor alpha	10956201
CHEMBL799981	11	Inhibition of [3H]-ATRA binding to Retinoic acid receptor alpha (RAR-alpha)	10956201
CHEMBL799980	11	Relative transcriptional activation in COS cells expressing Retinoic acid receptor alpha compared to ATRA	10956201
CHEMBL838382	1	Transcriptional activation in COS cells expressing RAR-alpha	10956201
CHEMBL802580	9	Percent activation of Retinoic acid receptor alpha at 1 uM relative to 1 uM trans-retinoic acid	10890153
CHEMBL801812	9	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor alpha	10890153
CHEMBL802579	7	Percent transcriptional activation of Retinoic acid receptor RAR alpha at 1 uM compared to 1 uM trans-retinoic acid	10890152
CHEMBL801811	7	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor RAR alpha	10890152
CHEMBL802577	2	Binding affinity for Retinoic acid receptor alpha relative to ATRA; Not detectable	10762039
CHEMBL802576	8	Binding affinity for Retinoic acid receptor alpha relative to ATRA	10762039
CHEMBL799873	1	Binding affinity for Retinoic acid receptor alpha	10762039
CHEMBL659135	1	Relative transcriptional activation in CV-1 cells expressing RAR alpha receptor compared to ATRA; Not detectable	10762039
CHEMBL659134	9	Relative transcriptional activation in CV-1 cells expressing RAR alpha receptor compared to ATRA	10762039
CHEMBL654646	1	Transcriptional activation in CV-1 cells expressing RAR alpha receptor	10762039
CHEMBL799757	4	Inhibition of [3H]ATRA-Hl60 binding to Retinoic acid receptor alpha relative to ATRA	10762038
CHEMBL802581	1	Relative binding affinity for Retinoic acid receptor alpha as IC50/IC50(ATRA)	10762038
CHEMBL799872	1	Inhibition of [3H]ATRA-Hl60 binding to Retinoic acid receptor alpha	10762038
CHEMBL659144	1	Relative transcriptional activation in CV-1 cells expressing RAR alpha receptor compared to ATRA; Not detectable	10762038
CHEMBL659143	4	Relative transcriptional activation in CV-1 cells expressing RAR alpha receptor compared to ATRA	10762038
CHEMBL654645	1	Transcriptional activation in CV-1 cells expressing RAR alpha receptor	10762038
CHEMBL799793	1	Binding affinity for Retinoic Acid Receptor alpha (RAR alpha).	10669568
CHEMBL799792	6	Binding affinity for Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL799791	3	Binding affinity for Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL799714	2	Induction of HL-60 cell differentiation at Retinoic Acid Receptor alpha (RAR	10669568

		alpha)	
CHEMBL800632	8	Transcriptional activation of Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL800631	2	Transcriptional activation of Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL799979	2	Binding affinity for Retinoic Acid Receptor alpha (RAR alpha);ND means not detectable.	10669568
CHEMBL799978	2	Binding affinity for Retinoic Acid Receptor alpha (RAR alpha);ND means not detectable.	10669568
CHEMBL698011	3	Transcriptional activation in COS-1 cells expressing Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL698008	1	Transcriptional activation in COS-1 cells expressing Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL688572	12	Induction of HL-60 cell differentiation at Retinoic Acid Receptor alpha (RAR alpha)	10669568
CHEMBL800770	1	Transcriptional activation of Retinoic acid receptor RAR alpha	10585206
CHEMBL798139	5	Transcriptional activation of Retinoic acid receptor RAR alpha; NA is Not Active	10585206
CHEMBL800328	6	In vitro binding affinity for Retinoic acid receptor RAR alpha	10585206
CHEMBL799860	1	Transcriptional activation of Retinoic acid receptor RAR alpha	10585206
CHEMBL799713	2	Transcriptional activation in CV-1 cells expressing human Retinoic acid receptor RAR alpha	10543887
CHEMBL798142	3	Percent transcriptional activation relative to 9-cis RA in CV-1 cells expressing Retinoic acid receptor RAR alpha	10479291
CHEMBL798140	3	Transcriptional activation in CV-1 cells expressing human Retinoic acid receptor alpha	10479291
CHEMBL846504	6	Binding affinity of [3H]- RA to baculovirus expressed human RAR alpha	10201840
CHEMBL846503	5	Relative inhibition of TTNPB activity vs background activity (100% inhibition) against RAR alpha	10201840
CHEMBL874059	5	Antagonistic activity against RAR alpha in transcriptional activation assay with 32 nM TTNPB	10201840
CHEMBL846502	1	Antagonistic activity against RAR alpha in transcriptional activation assay with 32 nM TTNPB; NT=Not tested	10201840
CHEMBL799718	4	Inhibition of [3H]RA binding to retinoic acid receptor RAR alpha	10098670
CHEMBL799874	16	Ability to displace 3[H](all-E)-retinoic acid (5 nM) from alpha retinoic acid receptor (alpha RAR) using transactivation assay	10098666
CHEMBL802572	4	Inhibition of [3H]ATRA binding to baculovirus expressed Retinoic acid receptor RAR alpha	10052980
CHEMBL799868	2	Percent transcriptional activation relative to ATRA in CV-1 cells expressing Retinoic acid receptor RAR alpha	10052980
CHEMBL799864	2	Transcriptional activation in CV-1 cells expressing Retinoic acid receptor RAR alpha	10052980

Tab. S13: Summary of the Protein Data Bank records for Retinoic Acid Receptor beta (RARb)

PDB ID	Structure title	PMID	Year Dep	Ligands used
1HRA	THE SOLUTION STRUCTURE OF THE HUMAN RETINOIC ACID RECEPTOR-BETA DNA-BINDING DOMAIN	8383553	1993	ZINC ION
1HRA	THE SOLUTION STRUCTURE OF THE HUMAN RETINOIC ACID RECEPTOR-BETA DNA-BINDING DOMAIN		1993	ZINC ION
1XAP	Structure of the ligand binding domain of the Retinoic Acid Receptor beta	15319780	2004	4-[(1E)-2-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRONAPHTHALEN-2-YL)PROP-1-ENYL]BENZOIC ACID
1XDK	Crystal Structure of the RARbeta/RXRalpha Ligand Binding Domain Heterodimer in Complex with 9-cis Retinoic Acid and a Fragment of the TRAP220 Coactivator	15528208	2004	(9cis)-retinoic acid
4DM6	Crystal structure of RARb LBD homodimer in complex with TTNPB	22355136	2012	4-[(1E)-2-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRONAPHTHALEN-2-YL)PROP-1-ENYL]BENZOIC ACID
4DM8	Crystal structure of RARb LBD in complex with 9cis retinoic acid	22355136	2012	RETINOIC ACID
4J5W	Crystal Structure of the apo-PXR/RXRalpha LBD Heterotetramer Complex	23602807	2013	MAGNESIUM ION
4JYG	Crystal structure of RARbeta LBD in complex with agonist BMS411 [4-{[(5,5-dimethyl-8-phenyl-5,6-	25933005	2013	2-{2-[2-(2-{2-[2-(2-ETHOXY-ETHOXY)-ETHOXY]-ETHOXY}-

	dihydronaphthalen-2-yl)carbonyl]amino}benzoic acid]			ETHOXY)-ETHOXY]-ETHOXY}-ETHANOL / 4-{[(5,5-dimethyl-8-phenyl-5,6-dihydronaphthalen-2-yl)carbonyl]amino}benzoic acid / CITRATE ANION
4JYH	Crystal structure of RARbeta LBD in complex with selective agonist BMS948 [4-{[(8-phenylnaphthalen-2-yl)carbonyl]amino}benzoic acid]	25933005	2013	4-{[(8-phenylnaphthalen-2-yl)carbonyl]amino}benzoic acid / CITRATE ANION
4JYI	Crystal structure of RARbeta LBD in complex with selective partial agonist BMS641 [3-chloro-4-[(E)-2-(5,5-dimethyl-8-phenyl-5,6-dihydronaphthalen-2-yl)ethenyl]benzoic acid]	25933005	2013	3-chloro-4-[(E)-2-(5,5-dimethyl-8-phenyl-5,6-dihydronaphthalen-2-yl)ethenyl]benzoic acid / CITRATE ANION
5UAN	Crystal structure of multi-domain RAR-beta-RXR-alpha heterodimer on DNA	29021580	2016	(9cis)-retinoic acid / RETINOIC ACID / ZINC ION
6SSQ	Crystal structure of RARbeta LBD in complex with LG 100754	31694317	2019	(2E,4E,6Z)-3-methyl-7-(5,5,8,8-tetramethyl-3-propoxy-5,6,7,8-tetrahydronaphthalen-2-yl)octa-2,4,6-trienoic acid / CITRATE ANION / GLYCEROL

Tab. S14: Summary of the ChEMBL records for Retinoic Acid Receptor beta (RARb)

Assay ID	Chem Ct	Assay Description	PMID
CHEMBL4401913	20	Transactivation of GAL4-fused mouse RARbeta-LBD expressed in COS-7 cells after 24 hrs by bright-Glo reagent based assay	30792038
CHEMBL4187006	1	Transactivation of mouse Gal4-fused RARbeta-LBD expressed in COS-7 cells after 1 day by bright-Glo reagent based assay	29288071
CHEMBL4187005	23	Transactivation of mouse Gal4-fused RARbeta-LBD expressed in COS-7 cells after 1 day by bright-Glo reagent based assay relative to control ATRA	29288071
CHEMBL3295538	3	Antagonist activity at Gal4-fused mouse RAR-beta transfected in human HeLa cells after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295531	3	Agonist activity at Gal4-fused mouse RAR-beta transfected in human HeLa cells at 1 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295528	1	Agonist activity at Gal4-fused mouse RAR-beta transfected in human HeLa cells at >1 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295526	3	Agonist activity at Gal4-fused mouse RAR-beta transfected in human HeLa cells at 10 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL1785132	7	Antagonist activity at yeast GAL4 fused mouse RARbeta ligand binding domain expressed in HeLa cells assessed as inhibition of TTNPB-induced receptor transactivation by luciferase reporter gene assay	19482478
CHEMBL1768347	2	Antagonist activity at mouse RARbeta expressed in COS-1 cells assessed as inhibition of Am80-induced transactivation by luciferase reporter gene assay	21459577
CHEMBL795961	1	Dissociation constant for binding to Retinoic acid receptor beta;NA=not active	8784454
CHEMBL795960	7	Dissociation constant for binding to Retinoic acid receptor beta	8784454
CHEMBL795959	8	Inhibition of binding to retinoid A receptor RAR beta	9572893
CHEMBL795958	6	Inhibition of murine Retinoic acid receptor RAR beta	7608895
CHEMBL795957	7	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR beta	9572893
CHEMBL795956	1	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR beta	9572893

Tab. S15: Summary of Protein Data Bank results for Retinoic Acid Receptor gamma (RARg)

PDB ID	Structure title	PMID	Year Dep	Ligands used
1EXA	ENANTIOMER DISCRIMINATION ILLUSTRATED BY CRYSTAL STRUCTURES OF THE HUMAN RETINOIC ACID RECEPTOR HRARGAMMA LIGAND BINDING DOMAIN: THE COMPLEX WITH THE ACTIVE R-ENANTIOMER BMS270394.	10841540	2000	DODECYL-ALPHA-D-MALTOSIDE / R-3-FLUORO-4-[2-HYDROXY-2-(5,5,8,8-TETRAMETHYL-5,6,7,8,-TETRAHYDRO-NAPHTALEN-2-YL)-ACETYLAMINO]-BENZOIC ACID
1EXX	ENANTIOMER DISCRIMINATION ILLUSTRATED BY CRYSTAL STRUCTURES OF THE HUMAN RETINOIC ACID	10841540	2000	3-FLUORO-4-[2-HYDROXY-2-(5,5,8,8-TETRAMETHYL-5,6,7,8,-TETRAHYDRO-NAPHTALEN-2-YL)-ACETYLAMINO]-

	RECEPTOR HRARGAMMA LIGAND BINDING DOMAIN: THE COMPLEX WITH THE INACTIVE S-ENANTIOMER BMS270395.			BENZOIC ACID / DODECYL-ALPHA-D-MALTOSIDE
1FCX	ISOTYPE SELECTIVITY OF THE HUMAN RETINOIC ACID NUCLEAR RECEPTOR HRAR: THE COMPLEX WITH THE RARGAMMA-SELECTIVE RETINOID BMS184394	10964567	2000	6-[HYDROXY-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRO-NAPHTALEN-2-YL)-METHYL]-NAPHTALENE-2-CARBOXYLIC ACID / DODECYL-ALPHA-D-MALTOSIDE
1FCY	ISOTYPE SELECTIVITY OF THE HUMAN RETINOIC ACID NUCLEAR RECEPTOR HRAR: THE COMPLEX WITH THE RARBETA/GAMMA-SELECTIVE RETINOID CD564	10964567	2000	6-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRO-NAPHTALENE-2-CARBONYL)-NAPHTALENE-2-CARBOXYLIC ACID / DODECYL-ALPHA-D-MALTOSIDE
1FCZ	ISOTYPE SELECTIVITY OF THE HUMAN RETINOIC ACID NUCLEAR RECEPTOR HRAR: THE COMPLEX WITH THE PANAGONIST RETINOID BMS181156	10964567	2000	4-[3-OXO-3-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRO-NAPHTHALEN-2-YL)-PROPENYL]-BENZOIC ACID / DODECYL-ALPHA-D-MALTOSIDE
1FD0	ISOTYPE SELECTIVITY OF THE HUMAN RETINOIC ACID NUCLEAR RECEPTOR HRAR: THE COMPLEX WITH THE RARGAMMA-SELECTIVE RETINOID SR11254	12220491	2000	6-[HYDROXYIMINO-(5,5,8,8-TETRAMETHYL-5,6,7,8-TETRAHYDRO-NAPHTALEN-2-YL)-METHYL]-NAPHTALENE-2-CARBOXYLIC ACID / DODECYL-ALPHA-D-MALTOSIDE
2LBD	LIGAND-BINDING DOMAIN OF THE HUMAN RETINOIC ACID RECEPTOR GAMMA BOUND TO ALL-TRANS RETINOIC ACID	7501014	1997	RETINOIC ACID
3LBD	LIGAND-BINDING DOMAIN OF THE HUMAN RETINOIC ACID RECEPTOR GAMMA BOUND TO 9-CIS RETINOIC ACID	9501913	1998	(9cis)-retinoic acid
4LBD	LIGAND-BINDING DOMAIN OF THE HUMAN RETINOIC ACID RECEPTOR GAMMA BOUND TO THE SYNTHETIC AGONIST BMS961	9501913	1998	3-FLUORO-4-[2-HYDROXY-2-(5,5,8,8-TETRAMETHYL-5,6,7,8,-TETRAHYDRO-NAPHTALEN-2-YL)-ACETYLAMINO]-BENZOIC ACID
5M24	RARg mutant-S371E	28125680	2016	(9cis)-retinoic acid / CHLORIDE ION / DODECYL-ALPHA-D-MALTOSIDE
6FX0	Structure-based design of Trifarotene (CD5789), a potent and selective RAR gamma agonist for the treatment of acne	29706423	2018	6-[3-(1-adamantyl)-4-oxidanyl-phenyl]naphthalene-2-carboxylic acid / TETRAETHYLENE GLYCOL

Tab. S16: Summary of ChEMBL results for Retinoic Acid Receptor gamma (RARg)

Assay ID	Chem Ct	Assay Description	PMID
CHEMBL3295539	3	Antagonist activity at Gal4-fused mouse RAR-gamma transfected in human HeLa cells after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295532	3	Agonist activity at Gal4-fused mouse RAR-gamma transfected in human HeLa cells at 1 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL3295527	3	Agonist activity at Gal4-fused mouse RAR-gamma transfected in human HeLa cells at 10 uM after 12 hrs by luciferase reporter gene assay	24900875
CHEMBL1785655	6	Agonist activity at yeast GAL4 fused mouse RARgamma ligand binding domain expressed in HeLa cells assessed as receptor transactivation by luciferase reporter gene assay	19482478
CHEMBL1785133	8	Antagonist activity at yeast GAL4 fused mouse RARgamma ligand binding domain expressed in HeLa cells assessed as inhibition of TTNPB-induced receptor transactivation by luciferase reporter gene assay	19482478
CHEMBL1768348	2	Antagonist activity at mouse RARgamma expressed in COS-1 cells assessed as inhibition of ATRA-induced transactivation by luciferase reporter gene assay	21459577
CHEMBL804940	1	Dissociation constant for binding to Retinoic acid receptor gamma;NA=not active	8784454
CHEMBL804939	7	Dissociation constant for binding to Retinoic acid receptor gamma	8784454
CHEMBL804938	8	Inhibition of binding to retinoid A receptor RAR gamma	9572893
CHEMBL804937	6	Inhibition of binding to murine Retinoic acid receptor RAR gamma	7608895
CHEMBL804936	1	Transcriptional activation in CV-1 cells expressing retinoic A receptor RAR gamma	9572893
CHEMBL804935	2	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR gamma	9572893
CHEMBL804934	1	Transcriptional activation in CV-1 cells expressing retinoid A receptor RAR gamma	9572893

Tab. S17: ToxCast and Tox21 results
Filtering of results is described in methods. Assays are organized by specific protein targets, metabolism targets, and testing the retinoid pathway in general. Descriptions of the assays can be found in Supplemental Table S18.

		Specific Targets					Metabolism		Pathway		
		RAR a	RAR b	RAR g	RAR	RAR	CYP 1A1	CYP 2C8			
DSSToxID	Chemical Name	ATG_RARa_trans_up	ATG_RARb_TRANS_up	ATG_RARg_TRANS_up	NVS_NR_hRAR_Agonist	NVS_NR_hRAR_Antagonist	NVS_ADME_hCYP1A1	NVS_ADME_hCYP2C8	ATG_DR5_CIS_up	Tox21_RAR_LUC_agonist	Tox21_RAR_LUC_antagonist
DTXSID7021239	all-trans-Retinoic acid				0.126		1.317		0.006		
DTXSID8024151	Imazalil	0.908					1.413				
DTXSID6020561	Endrin		1.606	1.698					0.806		
DTXSID9020453	Dieldrin	0.77		1.68					0.579		
DTXSID4038922	Tetrabromobisphenol A bis(2-hydroxyethyl) ether	1.503		0.84					0.22		
DTXSID3023556	Retinol	0.076		0.227					0.197		
DTXSID0020319	Chlorothalonil							0.182	0.185		
DTXSID2020347	Coumaphos						0.274		1.596		
DTXSID7032638	Pyraclostrobin						1.678		0.543		
DTXSID5040758	AM580			0.08					0.083	0.023	
DTXSID0048185	Apomorphine hydrochloride hydrate			1.802					1.683		
DTXSID2022880	Danazol	0.734							0.535		
DTXSID2032500	Triflumizole	1.453							#####		
DTXSID7047279	CP-532623	1.561							0.367		
DTXSID9037539	Endosulfan I	1.384							1.827		
DTXSID4024270	Prochloraz						0.413	1.679			
DTXSID9032329	Bensulide						0.551	0.662			
DTXSID0021385	Folpet							0.197			
DTXSID0032655	Triticonazole						0.793				
DTXSID1024259	Phosalone						0.489				
DTXSID2040363	Diniconazole						0.675				
DTXSID3020122	Azinphos-methyl						0.331				
DTXSID4020242	Captafol							0.091			
DTXSID4032372	Difenoconazole						1.459				
DTXSID4042121	Mepanipyrim						0.567				
DTXSID5020653	Gentian Violet						1.816				
DTXSID5032525	Bifenazate						0.484				
DTXSID8022325	2,2-Bis(4-hydroxyphenyl)-1,1,1-trichloroethane							1.835			
DTXSID9047259	1,3-Dichloro-6,7,8,9,10,12-hexahydroazepino[2,1-b] quinazoline hydrochloride (1:1)						0.791				
DTXSID9047598	4,4'-Sulfonylbis[2-(prop-2-en-1-yl)phenol]						1.946				
DTXSID6044519	1,1,3,3,5-Pentamethyl-4,6-dinitro-2,3-dihydro-1H-indene			1.606							
DTXSID2026602	2,4-Di-tert-butylphenol			1.514							
DTXSID7042065	Isodrin			1.077							
DTXSID8026193	1,2,3-Trichlorobenzene			0.953							

DTXSID8020040	Aldrin			0.912							
DTXSID0023901	Bentazone				1.899						
DTXSID2026523	Symclosene					0.264					
DTXSID4021559	2,6-Di-tert-butyl-4-nitrophenol	1.887									
DTXSID4024359	2,4,5-Trichlorophenol		1.058								
DTXSID7025895	N-Phenyl-1,4-benzenediamine		0.245								
DTXSID8037706	Potassium perfluorooctanesulfonate				1.912						
DTXSID8041379	2,6-Di-tert-butyl-4-methoxyphenol	1.071									
DTXSID8041909	Dysprosium(III) chloride					0.854					
DTXSID9022310	Daidzein				0.937						
DTXSID0023036	Etretinate									1.141	
DTXSID0033382	Daunomycin hydrochloride										1.6299
DTXSID0034223	Tebufenpyrad								0.48		
DTXSID0045173	Mitoxantrone dihydrochloride										0.1172
DTXSID0047379	SSR126768								0.423		
DTXSID0047797	Idarubicin hydrochloride										1.2778
DTXSID1020560	Endosulfan								0.894		
DTXSID1032488	Thiazopyr								1.305		
DTXSID1034501	gamma-Cyhalothrin								0.974		
DTXSID1040619	Bexarotene								0.014		
DTXSID1047368	SSR69071								1.011		
DTXSID2021311	2,4,6-Tris(tert-butyl)phenol								0.756		
DTXSID2032550	Fenpyroximate (Z,E)								0.026		
DTXSID2034625	Fluoxastrobin								0.577		
DTXSID2047272	CJ-013610								1.857		
DTXSID3020419	Dibutyltin diacetate										0.2183
DTXSID3020621	Fenvalerate								0.755		
DTXSID3024239	Oxadiazon								0.726		
DTXSID3042390	Sodium (2-pyridylthio)-N-oxide										0.5377
DTXSID3042500	Triphenyltin fluoride										0.0972
DTXSID4022153	Tetrabutyltin								0.279		
DTXSID4024276	Propargite								0.903		
DTXSID4040767	3,5-Dichlorosalicyl-3,4-dichloroanilide								1.199		
DTXSID4047383	AVE3247								1.38		
DTXSID4048511	PharmaGSID_48511								0.546		
DTXSID4048519	PharmaGSID_48519								1.222		
DTXSID5021463	Zinc diethyldithiocarbamate										1.2383
DTXSID5025998	Retinal									0.504	
DTXSID5032573	Pyridaben								1.103		
DTXSID5034981	Tributyltin benzoate								0.023		
DTXSID5046481	Adapalene									0.033	
DTXSID5046691	Tazarotene									0.438	
DTXSID5046776	Ataluren										0.5982
DTXSID5046853	Tamibarotene									0.158	
DTXSID5047322	SB243213A								1.289		
DTXSID6020690	Hexachlorophene								0.714		
DTXSID6021248	Rotenone								0.022		
DTXSID6021408	Triphenyltin acetate										0.0408
DTXSID6025513	Malachite green oxalate										0.4936
DTXSID7020267	Chlordane								1.784		
DTXSID7020558	Emetine dihydrochloride										0.1883

DTXSID7022883	Daunorubicin										0.9245
DTXSID7026314	Zinc pyrithione										0.0241
DTXSID7029241	2,4-Bis(1-methyl-1-phenylethyl)phenol								1.863		
DTXSID8020381	Deltamethrin								0.545		
DTXSID8024238	Oryzalin								1.116		
DTXSID8034401	Buprofezin								1.084		
DTXSID8035180	Allethrin								0.746		
DTXSID8047347	SR271425								0.419		
DTXSID9021342	Bithionol								1.807		
DTXSID9032379	Dithiopyr								1.187		
DTXSID9032533	Chlorfenapyr								0.503		
DTXSID9034997	Tributyltetradecylphosphonium chloride								1.307		
DTXSID9040760	{4-[({2-[3-Fluoro-4-(trifluoromethyl)phenyl]-4-methyl-1,3-thiazol-5-yl}methyl)sulfanyl]-2-methylphenoxy}acetic acid								0.896		
DTXSID9044796	(Acryloyloxy)(tributyl)stannane								0.022		
DTXSID9046992	Nicardipine hydrochloride								0.283		
DTXSID9048512	Ro 23-7637								1.365		
DTXSID9058654	BisOPP-A								0.736		

Tab. S18: Descriptions of ToxCast / Tox21 assays

Name	Active	Total	Description
ATG_RARa_TRANS_up	80	3807	Data from the assay component ATG_RARa_TRANS was analyzed into 1 assay endpoint. This assay endpoint, ATG_RARa_TRANS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, measures of mRNA for gain-of-signal activity can be used to understand the reporter gene at the transcription factor-level as they relate to the gene RARA. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a reporter gene function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "non-steroidal".
ATG_RARb_TRANS_up	26	3807	Data from the assay component ATG_RARb_TRANS was analyzed into 1 assay endpoint. This assay endpoint, ATG_RARb_TRANS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, measures of mRNA for gain-of-signal activity can be used to understand the reporter gene at the transcription factor-level as they relate to the gene RARB. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a reporter gene function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "non-steroidal".
ATG_RARb_TRANS_dn	152	3807	ATG_RARb_TRANS_dn was not developed or optimized to detect loss of signal. Use data with caution.
ATG_RARg_TRANS_up	63	3807	Data from the assay component ATG_RARg_TRANS was analyzed into 1 assay endpoint. This assay endpoint, ATG_RARg_TRANS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, measures of mRNA for gain-of-signal activity can be used to understand the reporter gene at the transcription factor-level as they relate to the gene RARG. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a reporter gene function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "non-steroidal".
ATG_RARg_TRANS_dn	82	3807	ATG_RARg_TRANS_dn was not developed or optimized to detect loss of signal. Use data with caution.
TOX21_RAR_LUC_Agonist	305	7521	Data from the assay component TOX21_RAR_LUC_Agonist was analyzed into 1 assay endpoint. This assay endpoint, TOX21_RAR_LUC_Agonist, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, gain-of-signal activity can be used to understand changes in the reporter gene as they relate to the gene RARA.

			Furthermore, this assay endpoint can be referred to as a primary readout, because the performed assay has only produced 1 assay endpoint. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the nuclear receptor intended target family.
TOX21_RAR_LUC_Antagonist	985	7871	Data from the assay component TOX21_RAR_LUC_Antagonist was analyzed into 1 assay endpoint. This assay endpoint, TOX21_RAR_LUC_Antagonist, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, loss-of-signal activity can be used to understand changes in the reporter gene as they relate to the gene RARA. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a reporter gene function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the nuclear receptor intended target family.
ATG_DR5_CIS_up	339	3807	Data from the assay component ATG_DR5_RAR_CIS was analyzed into 1 assay endpoint. This assay endpoint, ATG_DR5_CIS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, measures of mRNA for gain-of-signal activity can be used to understand the reporter gene at the transcription factor-level as they relate to the gene RARA and RARB and RARG. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a reporter gene function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "non-steroidal".
ATG_DR5_CIS_dn	153	3807	ATG_DR5_CIS_dn was not developed or optimized to detect loss of signal. Use data with caution
NVS_ADME_hCYP1A1	111	1124	Data from the assay component NVS_ADME_hCYP1A1 was analyzed into 2 assay endpoints. This assay endpoint, NVS_ADME_hCYP1A1, was analyzed in the positive fitting direction relative to Acetonitrile as the negative control and baseline of activity. Using a type of enzyme reporter, loss-of-signal activity can be used to understand changes in the enzymatic activity as they relate to the gene CYP1A1. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a enzymatic activity function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "cyp" intended target family, where the subfamily is "xenobiotic metabolism".
NVS_ADME_hCYP2C8	24	315	Data from the assay component NVS_ADME_hCYP2C8 was analyzed into 2 assay endpoints. This assay endpoint, NVS_ADME_hCYP2C8, was analyzed in the positive fitting direction relative to Acetonitrile as the negative control and baseline of activity. Using a type of enzyme reporter, loss-of-signal activity can be used to understand changes in the enzymatic activity as they relate to the gene CYP2C8. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a enzymatic activity function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "cyp" intended target family, where the subfamily is "xenobiotic metabolism".