



Expert Group on Retinoid Pathway Signaling
Advisory Group on Endocrine Disruptors Testing and Assessment (EDTA), Test Guidelines Program
OECD Headquarters, Paris
November 12-14, 2019



Retinoid Pathway Signaling:

Identification and support for candidate reference chemicals

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DISCLAIMER: The views expressed are those of the presenter and do not necessarily reflect Agency policy.

Thank you to contributors

EPA-Virtual Tissue Models



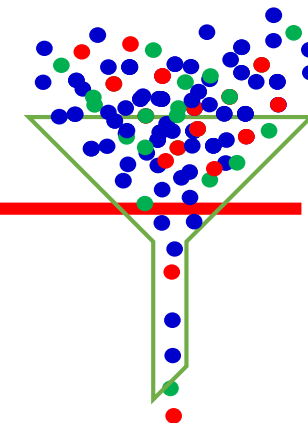
- Tom Knudsen - CCTE
- Todd Zurlinden –CCTE
- Kate Saili –CCTE (now EPA/OAQPS)
- Chad Deisenroth – CCTE
- Richard Spencer - ARA / EMVL
- Bhavesh Ahir - CCTE / ORISE (now Eurofins)
- Richard Judson - CCTE
- Ann Richard – CCTE
- Antony Williams - CCTE

DRP-Retinoid system



- Patience Browne – TGP and Team
- OECD/EC Retinoid DRP group / Brussels

Goals of this presentation



- Background: *reference chemicals*
 - Key to testing / interrogating / interpreting aspects of the retinoid signaling pathway (e.g., *in vitro* data, *in silico* models) essential for predictive toxicology.
 - Identifying the right chemical compounds from available resources (e.g., literature, databases) and ‘sifting’ the information around them is challenging.
- Goals:
 - Assemble collections of candidate reference chemicals that convey important information on the underlying biology of retinoid signaling (2 tools).
 - Provide a tool that can be easily used to investigate / organize evidence extracted from the relevant literature ([Abstract Sifter](#) [Baker et al. 2017]).

Identify Chemicals

Sources

ToxCast

ToxCast_RetinoidPathway.xlsm

LitDB

LitDB_RetinoidPathway.xlsm

What delivered?

Investigate

What delivered?

AbstractSifter_RetinoidPathway.xlsm

A		B		C		D		E		F		G		H		I		J	
1		Abstract Sifter		Query PubMed						Query run: (E555-44-0 OR imazali OR eniconazole) AND (retinoic acid OR tretinoin) AND (drug effects OR metabolism OR regulation OR regulate)								Provided by the USEPA's National Center for Computational Toxicology	
2		v4		Your filter terms and frequency counts															
				ret		rare		retinol		Total		Pub		Yr		Title			
3		PMID																PMC	
4		22289359		7						7		14		2012		Inhibitory effects of azole-type fungicides on interleukin-17 gene expression via retinoic acid receptor-related orphan receptor		Authors	
5		13124165		3						3		6		2009		Effects of the azole fungicide imazali on the development of the ascidian Ciona intestinalis (Chordata, Tunicata): morphological and molecular analysis		Zega G, De Bernardi F, Groppelli S, FA	
6		1727381		4						4		8		2007		Cital, an inhibitor of retinoic acid synthesis, attenuates the frequency and severity of branchial arch abnormalities induced by retinoic acid		Di Renzo F, Brocca ML, Giavini S, M R	
7		16863669		2						2		4		2006		Toxic effects of two pesticides, imazali and Tridimefon, on the early development of the ascidian Phallusia mammillata		Pennati R, Groppelli S, Zega G, Bigli A	
8		16139706		3						3		6		2006		Dysmorphogenic effects of some fungicides derived from the imidazole on rat embryos cultured in vitro		Menegola E, Brocca ML, Di Renzo F, R	

A		B		C		E		F		G		H		I	
Abstract Sifter		Landscape View													
		Update Article Counts		View / Hide queries		Heat Map by column		Heat Map by row							
2															
3															
4															

Example 1: retinoid pathway candidates from ToxCast

- Download assay data from CompTox Chemicals Dashboard to database
- Combine and organize
- Output to Excel
 - Add overview
 - Add navigation

ToxCast/Tox21 Assay	Target
atg_dr5_cis_dn	dr5
atg_dr5_cis_up	dr6
atg_rara_trans_dn	rara
atg_rara_trans_up	rara
atg_rarb_trans_dn	rarb
atg_rarb_trans_up	rarb
atg_rarg_trans_dn	rarg
atg_rarg_trans_up	rarg
atg_rxra_trans_dn	rxra
atg_rxrb_trans_dn	rxrb
nvs_adme_hcyp1a1	cyp1a1
nvs_adme_rcyp1a1	cyp1a1
nvs_nr_hrar_antagonist	rar
nvs_nr_hrara_agonist	rara
tox21_rar_luc_agonist	rar
tox21_rar_luc_antagonist	rar

ToxCast_RetinoidPathway.xlsm

Link to
CompTox
Chemicals
Dashboard
->

	A	C	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
1	ToxCast Overview																	
2			ToxCast hit calls															
3	DTXSID	PREFERRED_NAME	atg_df5_cis_dn	atg_df5_cis_up	atg_rara_trans_dn	atg_rara_trans_up	atg_rarb_trans_dn	atg_rarb_trans_up	atg_rarg_trans_dn	atg_rarg_trans_up	atg_rxxa_trans_dn	atg_rxxb_trans_dn	nvs_adme_hcyp1a1	nvs_adme_rcyp1a1	nvs_nr_hrar_antagonist	nvs_nr_hrara_antagonist	tox21_rar_luc_antagonist	tox21_rar_luc_antagonist
4	DTXSID1026902	N,N,N-Trimethyloctadecan-1-aminium chloride	0	1	0	1	0	1	0	1	0	1	0	0	0	0	0	1
5	DTXSID1040619	Bexarotene	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1
6	DTXSID2021103	Pentachloroanisole	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0
7	DTXSID2022880	Danazol	0	1	0	1	1	0	0	1	0	0	0	0	0	0	0	1
8	DTXSID2024585	Benzo(f)quinoline	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0
9	DTXSID2032342	Chinomethionate	0	1	0	1	0	0	0	1	0	1	0	0	0	0	0	0
10	DTXSID3023556	Retinol	0	1	0	1	0	0	0	1	0	0	0	0	0	0	1	0
11	DTXSID3025091	3,3'-Dimethoxybenzidine	0	1	0	1	0	0	0	1	1	0	1	0	0	0	0	0
12	DTXSID4038922	Tetrabromobisphenol A bis(2-hydroxyethyl) ethe	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1
13	DTXSID5037028	Hexadecyltrimethylammonium bromide	0	1	0	1	0	1	0	1	0	0	0	0	1	0	0	1
14	DTXSID7020687	1,2,3,4,5,6-Hexachlorocyclohexane	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1
15	DTXSID7038864	2,2'-Methylenebis(ethyl-6-tert-butylphenol)	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1
16	DTXSID7047306	CP-634384	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0
17	DTXSID9020453	Dieldrin	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	1
18	DTXSID9032531	Bromuconazole	0	1	0	1	0	0	0	1	0	1	0	0	0	0	0	1
19	DTXSID9044582	1-tert-Butyl-3,4,5-trimethyl-2,6-dinitrobenzene	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0
20	DTXSID0020022	Acifluorfen	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
21	DTXSID0024002	Fenpropathrin	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
22	DTXSID0032572	Prallethrin	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1
23	DTXSID0051493	2,3-Diaminopyridine	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
24	DTXSID1023998	Cypermethrin	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
25	DTXSID1024259	Phosalone	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
26	DTXSID1027924	Diisodecyl hexanedioate	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
27	DTXSID1046970	5HPP-33	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1

<- Assays

<- Hit calls

To use this tool, sort and browse, then double-click on blue cell to see detail

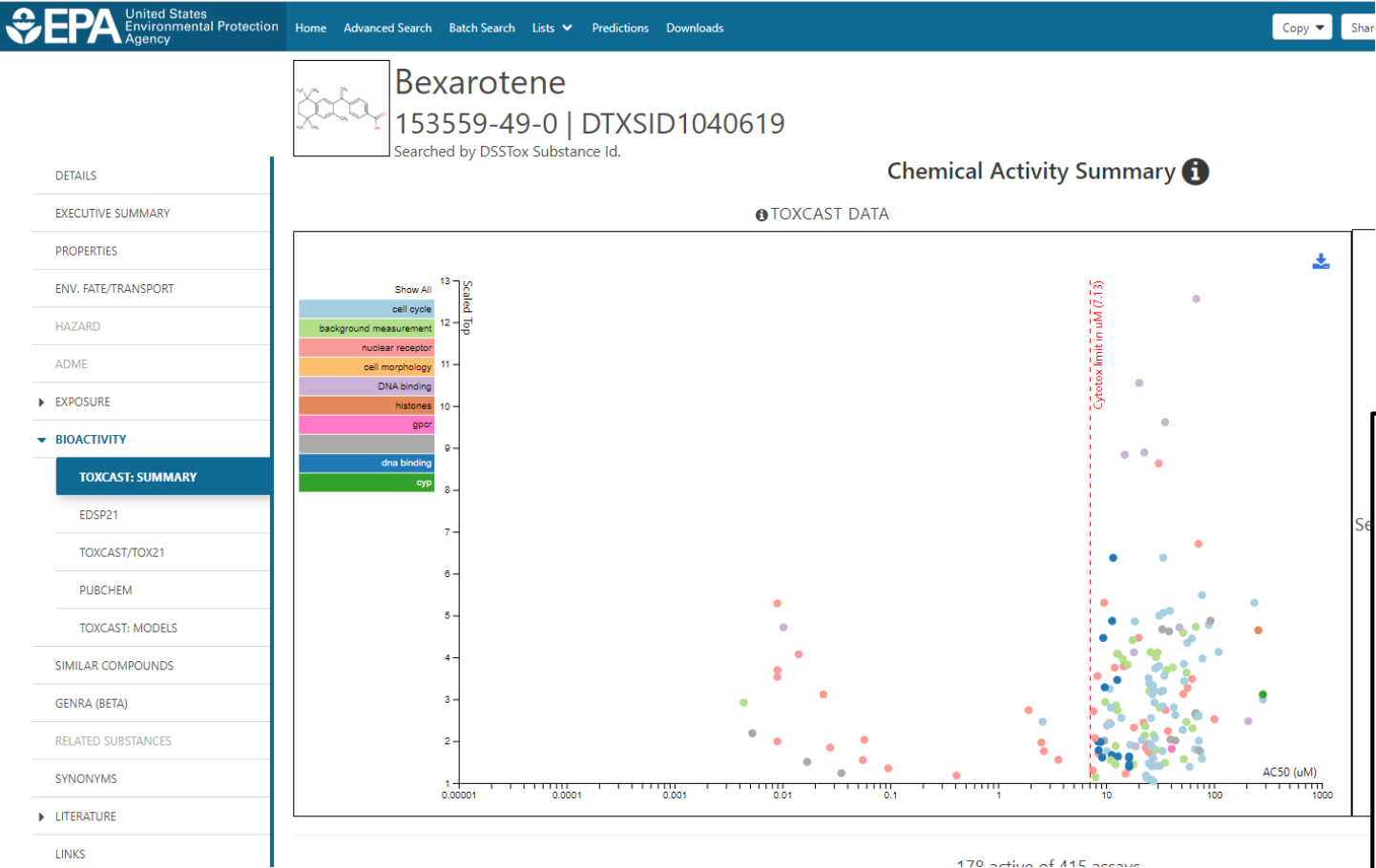
Detail sheet

	A	B	C	E	G	H
1	Detail	<-- Back				
2	DTX Link	Preferred Name	ToxCast Assay	Pct ToxCast	scaled top	AC50
911	DTXSID0025789	beta-Nitrostyrene	tox21_rar_luc_antagonist	235 / 586	3.399090076	27.65681
912	DTXSID1040619	Bexarotene	atg_dr5_cis_up	178 / 415	4.071380658	0.014157
913	DTXSID1040619	Bexarotene	atg_rara_trans_up	178 / 415	1.298254694	7.539354
914	DTXSID1040619	Bexarotene	atg_rarg_trans_up	178 / 415	1.757510318	2.655007
915	DTXSID1040619	Bexarotene	tox21_rar_luc_antagonist	178 / 415	2.031132273	0.057424
916	DTXSID5032525	Bifenazate	nvs_adme_hcyp1a1	127 / 826	3.150054724	0.484242
917	DTXSID9040269	Binapacryl	atg_dr5_cis_up	232 / 576	1.741752336	40.14372
918	DTXSID9040269	Binapacryl	tox21_rar_luc_antagonist	232 / 576	2.270558915	32.8007
919	DTXSID1022394	Biochanin A	tox21_rar_luc_agonist	143 / 470	1.366423228	1.058868
920	DTXSID4020161	Biphenyl	atg_rarg_trans_dn	20 / 671	1.132079577	100.0153
921	DTXSID9047174	Bis(2-butoxyethyl) phthalate	tox21_rar_luc_antagonist	50 / 400	1.917641236	79.59006
922	DTXSID9020168	Bis(2-chloroethyl) ether	atg_dr5_cis_up	8 / 705	1.326809406	0.616579
923	DTXSID2027094	Bis(2-ethylhexyl) maleate	atg_dr5_cis_dn	49 / 602	2.994099845	91.49065

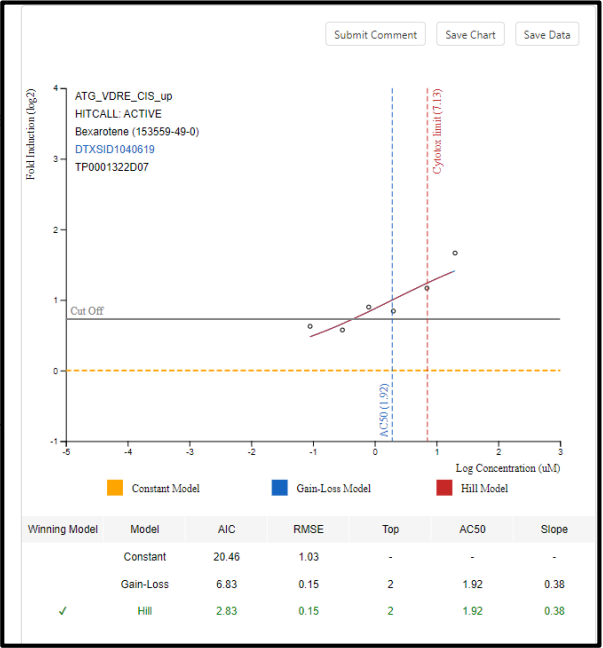
Link to
Dashboard
for details ->

CompTox Chemicals Dashboard

Use the DSSToxID hyperlink to come here to see chemical and assay information.




ToxCast data on the Dashboard



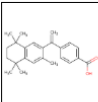
SOURCE: <https://comptox.epa.gov/dashboard>

CompTox Chemicals Dashboard

United States Environmental Protection Agency

HomeAdvanced SearchBatch SearchLists▼PredictionsDownloads

CopyShar



Bexarotene

153559-49-0 | DTXSID1040619

Searched by DSSTox Substance Id.

DETAILS

EXECUTIVE SUMMARY

PROPERTIES

ENV. FATE/TRANSPORT

HAZARD

ADME

EXPOSURE

BIOACTIVITY

TOXCAST: SUMMARY

EDSP21

TOXCAST/TOX21

PUBCHEM

TOXCAST: MODELS

SIMILAR COMPOUNDS

GENRA (BETA)

RELATED SUBSTANCES

SYNONYMS

LITERATURE

LINKS

Chemical Activity Summary ⓘ

178 active of 415 assays

DownloadColumns10Search queryShow InactiveShow Background

Name	Modal	SeqAPASS	Gene Symbol	AOP	Event	Hit Call	Top	AC50	logAC50	MaxMed	Cutoff	ModIAcc	Intended Target Family
ATG_DR5_CIS_up		NP_001277145.1	RARB	-	-	ACTIVE	2.41	1.42e-2	-1.85	3.05 - log ₂ _fold_induction	0.592	-2.53	nuclear receptor
ATG_EGR_CIS_up		NP_001955.1	EGR1	-	-	ACTIVE	1.37	8.90	0.950	1.14 - log ₂ _fold_induction	0.692	0.955	dna binding
ATG_ERE_CIS_up		NP_000116.2	ESR1	200	1181	ACTIVE	0.780	5.57e-2	-1.25	0.767 - log ₂ _fold_induction	0.503	-1.05	nuclear receptor
ATG_HSE_CIS_up		NP_005517.1	HSF1	-	-	ACTIVE	2.13	9.43	0.975	2.12 - log ₂ _fold_induction	0.476	0.907	dna binding
ATG_IR1_CIS_up		NP_001193922.1	NR1H4	61	479	ACTIVE	1.52	2.40e-2	-1.62	1.47 - log ₂ _fold_induction	0.488	-2.25	nuclear receptor
ATG_MRE_CIS_up		NP_005946.2	MTF1	-	-	ACTIVE	2.93	11.4	1.06	2.44 - log ₂ _fold_induction	0.601	0.850	dna binding
ATG_Oct_MLP_CIS_up		NP_002688.3	POU2F1	-	-	ACTIVE	1.16	11.3	1.05	0.971 - log ₂ _fold_induction	0.699	1.12	dna binding
ATG_Pax6_CIS_up		NP_000271.1	PAX6	-	-	ACTIVE	1.11	8.55	0.932	1.11 - log ₂ _fold_induction	0.623	0.945	dna binding
ATG_PPRE_CIS_up		NP_005027.2	PPARA	58	468	ACTIVE	1.79	9.00e-3	-2.05	2.32 - log ₂ _fold_induction	0.900	-2.03	nuclear receptor
ATG_PXRE_CIS_up		NP_071285.1	NR1I2	60	245	ACTIVE	0.786	0.412	-0.386	0.808 - log ₂ _fold_induction	0.669	-0.130	nuclear receptor

First<<<12345678910>>>Last

1

AC50 (uM)

0.000010.00010.0010.010.11101001000

170 active of 415 assays

Identify Chemicals

Sources

ToxCast

LitDB

What delivered?

ToxCast_RetinoidPathway.xlsm

LitDB_RetinoidPathway.xlsm

Investigate

What delivered?

AbstractSifter_RetinoidPathway.xlsm

A		B		C		D		E		F		G		H		I		J	
1		Abstract Sifter		Query PubMed						Query run: (33554-44-0 OR imazali OR eniconazole) AND ((retinoic acid OR tretinoin) AND (drug effects OR metabolism OR regulation OR regulate))								Provided by the USEPA's National Center for Computational Toxicology	
2		v4		Your filter terms and frequency counts															
				ret		rare		retinol		Total		Pub		Yr		Title			
3		PMID																	
4		22289359		7		0		7		14		2012							
5		13124165		3		0		3		6		2009							
6		1727381		4		0		4		8		2007							
7		16863665		2		0		2		4		2006							
8		16135706		3		0		3		6		2006							

A		B		C		D		E	F	G	H	I	
Abstract Sifter		Landscape View											
		Update Article Counts		View / Hide queries		Heat Map by column		Heat Map by row					
2													

Example 2: retinoid pathway candidates from PubMed MeSH

- Using the EPA LitDB (a database of MeSH terms from PubMed articles)
 - Extract MeSH annotations for retinoid pathway targets
 - Find the articles in which the target or its parent is annotated with either *agonists* or *antagonists & inhibitors*
- Organize and process
- Output to Excel
 - Add overview
 - Add navigation

LitDB_RetinoidPathway.xlsm tool: what it is and how to use

	A	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS	AT	AU	AV	AW	AX	AY	AZ	BA	BB		
1	Overview																																																					
2	Double-click on article count to see detail																																																					
	Targets and direction ->	Cyp26 a1 protein, mouse/ant	Cyp26 b1 protein, mouse/ant	cyp26 a1 protein, zebrafish/ant	Retinoic Acid 4-Hydroxylase/ant	retinol dehydrogenase/ant	retinol-palmitate esterase/ant	lecithin-retinol acyltransferase/ant	retinoic acid receptor beta/ag	retinoic acid receptor beta/ant	retinoic acid receptor beta2, mouse/ag	retinoic acid receptor gamma/ag	retinoic acid receptor gamma/ant	retinol dehydratase/ant	retinol dehydrogenase 5 /ant	ALDH2 protein, human/ant	RALDH2 protein, mouse/ant	ALDH3A1 protein, human/ant	ALDH5A1 protein, human/ant	Aldh5 a1 protein, rat/ant	cyp26 b1 protein, zebrafish/ant	Aldh2 protein, rat/ag	Aldh2 protein, rat/ant	retinaldehyde dehydrogenase 3, mouse/ant	ALDH1A1 protein, human/ant	ALDH1A1 protein, mouse/ant	ALDH2 protein, mouse/ant	Raldh2 protein, zebrafish/ant	RALDH1 protein, rat/ant	ALDH1L1 protein, human/ant	retinoic acid receptor, beta2, human/ag	retinoic acid receptor, beta2, human/ant	ALDH1A2 protein, human/ant	Retinoic Acid Receptor alpha/ag	Retinoic Acid Receptor alpha/ant	Alcohol Oxidoreductases/ant	Aldehyde Dehydrogenase/ant	Receptors, Retinoic Acid/ag	Receptors, Retinoic Acid/ant	Retinoid X Receptors/ag	Retinoid X Receptors/ant	Retinoid X Receptor alpha/ag	Retinoid X Receptor alpha/ant	Retinoid X Receptor gamma/ag	Retinoid X Receptor beta/ag	Retinoid X Receptor beta/ant	Retinal Dehydrogenase /ant	Retinol-Binding Proteins/ant	Retinol O-Fatty-Acyltransferase/ant	Retinol-Binding Proteins, Plasma/ag	Retinol-Binding Proteins, Plasma/ant	Retinol-Binding Proteins, Cellular/ant		
4	MeSH Chemical Name (hyperlinked)																																																					
5	Tretinoin	1	1	1	1	2	0	0	9	16	0	10	6	0	0	0	2	0	0	0	1	0	0	0	1	2	0	1	0	0	0	1	0	34	29	2	5	106	87	59	16	5	5	0	1	0	7	1	0	0	1	0		
6	Am 580	0	0	0	0	0	0	0	2	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11	0	0	0	13	2	3	0	0	0	0	0	0	0	0	0	0	0	0		
7	tamibarotene	0	0	0	0	0	0	0	4	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0	16	1	1	0	0	0	0	0	0	0	0	0	0	0	0		
8	Alitretinoin	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2	0	0	24	6	35	2	2	2	0	0	0	1	0	0	0	0	0		
9	ER 38925	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
10	AGN 193836	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	
11	CD 437	0	0	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	6	3	2	0	0	0	0	0	0	0	0	0	0	0	0		
12	ER 34617	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
13	Iuffariellolide	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
14	Vitamin A	0	0	0	0	1	3	4	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	8	0	7	5	3	1	0	0	0	0	0	1	1	2	1	0	1		
15	3,7-dimethyl-9-ferrocenylnona-2,4,6,8-tetraenoic acid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
16	4-(2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	7	6	4	2	0	0	0	0	0	0	0	0	0	0	0	0	
17	4-(5-(7-fluoro-4-(trifluoromethyl)benzo(b)furan-2-yl)-1H-2-pyr	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Article Counts

Chemical name (hyperlinked to MeSH)

Detail sheet has links to the PubMed citation

	A	B	I	K	L	M
1	Detail	<-- Back				
2	Chemical Name (hyperlinked)	Protein / Target (hyperlinked)	Act	PMID	Pub Yr	Title
537	Am 580	Receptors, Retinoic Acid	ant	8284797	1994	A retinoic acid receptor alpha antagonist counteracts retinoid teratogenicity in vitro
538	Am 580	Receptors, Retinoic Acid	ag	8759622	1996	Identification of a retinoic acid receptor alpha subtype specific agonist.
539	Am 580	Receptors, Retinoic Acid	ag	9439352	1998	A retinoic acid receptor-alpha (RAR alpha) selective agonist modulates procoagulant
540	Am 580	Retinoic Acid Receptor alpha	ag	11726401	2001	Effects of retinoic acid receptor-selective agonists on human nasal epithelial cell dif
541	Am 580	Retinoic Acid Receptor alpha	ag	12169446	2002	Enhancement of the inducible NO synthase activation by retinoic acid is mimicked b
542	Am 580	Retinoic Acid Receptor alpha	ag	17290005	2007	A widely used retinoic acid receptor antagonist induces peroxisome proliferator-act
543	Am 580	Retinoic Acid Receptor alpha	ag	19790202	2009	Synthesis and pharmacological characterization of Disila-AM80 (Disila-tamibarotene
544	Am 580	Retinoic Acid Receptor alpha	ag	20453882	2010	Mechanism of inhibition of MMTV-neu and MMTV-wnt1 induced mammary oncoger
545	Am 580	Retinoic Acid Receptor alpha	ag	22258322	2012	Roflumilast enhances the renal protective effects of retinoids in an HIV-1 transgenic
546	Am 580	Retinoic Acid Receptor alpha	ag	22920668	2012	Reversal by RAR α agonist Am580 of c-Myc-induced imbalance in RAR α /RAR γ expres
547	Am 580	Retinoic Acid Receptor alpha	ag	28780376	2017	Retinoic acid induction of CD1d expression primes chronic lymphocytic leukemia B c
548	Am 580	Retinoic Acid Receptor alpha	ag	29288071	2018	Design and synthesis of a potent, highly selective, orally bioavailable, retinoic acid r
549	Am 580	Retinoic Acid Receptor alpha	ag	8759622	1996	Identification of a retinoic acid receptor alpha subtype specific agonist.
550	Am 580	Retinoic Acid Receptor alpha	ag	9439352	1998	A retinoic acid receptor-alpha (RAR alpha) selective agonist modulates procoagulant
551	Am 580	retinoic acid receptor beta	ag	11726401	2001	Effects of retinoic acid receptor-selective agonists on human nasal epithelial cell dif
552	Am 580	retinoic acid receptor beta	ag	29288071	2018	Design and synthesis of a potent, highly selective, orally bioavailable, retinoic acid r
553	Am 580	retinoic acid receptor gamma	ag	11726401	2001	Effects of retinoic acid receptor-selective agonists on human nasal epithelial cell dif
554	Am 580	retinoic acid receptor gamma	ag	22920668	2012	Reversal by RAR α agonist Am580 of c-Myc-induced imbalance in RAR α /RAR γ expres
555	Am 580	retinoic acid receptor gamma	ag	28418498	2017	Suppression by an RAR- γ Agonist of Collagen Degradation Mediated by Corneal Fibr
556	Am 580	retinoic acid receptor gamma	ag	29288071	2018	Design and synthesis of a potent, highly selective, orally bioavailable, retinoic acid r

Identify Chemicals

Sources

ToxCast

LitDB

What delivered?

ToxCast_RetinoidPathway.xlsm

LitDB_RetinoidPathway.xlsm

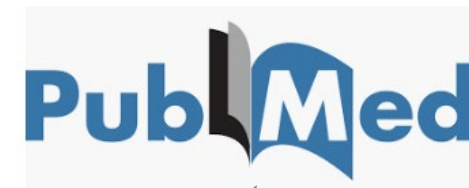
Investigate

What delivered?

AbstractSifter_RetinoidPathway.xlsm

PubMed Abstract Sifter

- Publicly available tool developed at US EPA
- Custom version for this project: AbstractSifter_RetinoidPathway.xlsm
- What is an Abstract Sifter?
 - Excel front end to PubMed
 - Works only in Windows (Sorry, Mac users)
- Citations can be
 - Retrieved, sorted, searched, and sifted
 - Tagged and noted
 - Exported



Internet

Abstract Sifter

Landscape View

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PubMed Abstract Sifter – quick overview – Main sheet

[illegible]

PubMed Abstract Sifter – Landscape sheet

1	Abstract Sifter	Landscape View							
2			Update Article Counts	View / hide queries	Heat Map by column	Heat Map by row			
3									
4									
5									
6	DTXSID2021781	Dibutyl phthalate	84-74-2 OR Dibutyl phthalate	any	1mie	2ke	3ke	4ao	
7	DTXSID5031131	Dipentyl phthalate **	131-18-0 OR Dipentyl phthalate OR di-n-pentyl phthalate	63	0	12	0	0	
8	DTXSID5020607	Di(2-ethylhexyl) phthalate **	117-81-7 OR Di(2-ethylhexyl) phthalate OR Diethylhexyl Phthalate	3949	0	384	0	2	
9	DTXSID5040758	AM580	102121-60-8 OR AM580 OR Am 580	136	28	61	0	5	
10	DTXSID5046481	Adapalene	106685-40-9 OR Adapalene	497	4	23	0	1	
11	DTXSID0021963	4-(Diethylamino)benzaldehyde	120-21-8 OR 4-(Diethylamino)benzaldehyde	30	2	5	0	0	
12	DTXSID80154737	Cd 437	125316-60-1 OR Cd 437	114	11	41	0	1	
13	DTXSID70439469	CHEMBL37708	155877-83-1 OR CHEMBL37708	0	0	0	0	0	
14	DTXSID80168213	BMS453	166977-43-1 OR BMS453	11	8	8	0	1	
15	DTXSID10886034	2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, (2E,4E)-	53092-52-7 OR 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, (2E,4E)-	0	0	0	0	0	
16	DTXSID6022553	Acitretin	55079-83-9 OR Acitretin	1671	4	37	0	9	
17	DTXSID6040743	Arotinoid acid	71441-28-6 OR Arotinoid acid OR 4-(2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-	0	0	0	0	0	
18	DTXSID50472965	AGN 193109	171568-43-7 OR AGN 193109	40	30	16	0	2	
19	DTXSID30								13
20	DTXSID00								13
21	DTXSID30								4
22	DTXSID70								4

The Landscape sheet provides an overview.

Article counts

PubMed Abstract Sifter – Landscape sheet

PubMed Query

×

Abstract Sifter

Landscape View

1

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DSSTOX link to Dashboard

Preferred Name

DTXSID2021781

Dibutyl phthalate

DTXSID5031131

Dipentyl phthalate **

DTXSID5020607

Di(2-ethylhexyl) phthalate

DTXSID5040758

AM580

DTXSID5046481

Adapalene

DTXSID0021963

4-(Diethylamino)benzaldehyde

DTXSID80154737

Cd 437

DTXSID70439469

CHEMBL37708

DTXSID80168213

BMS453

DTXSID10886034

2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, (2E,4E)-

DTXSID6022553

Acitretin

DTXSID6040743

Arotinoid acid

DTXSID50472965

AGN 193109

DTXSID30

DTXSID00

DTXSID30

DTXSID70

102121-60-8 OR AM580 OR Am 580

106685-40-9 OR Adapalene

120-21-8 OR 4-(Diethylamino)benzaldehyde

125316-60-1 OR Cd 437

155877-83-1 OR CHEMBL37708

166977-43-1 OR BMS453

53092-52-7 OR 2,4-Dodecadienoic acid, 11-methoxy-3,7,11-trimethyl-, (2E,4E)-

55079-83-9 OR Acitretin

71441-28-6 OR Arotinoid acid OR 4-(2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-

171568-43-7 OR AGN 193109

When this form goes away, your query is done.

Submit

Delete then add

Append

OR cleft lip OR skull OR jaw OR craniofacial anomaly OR cleft face or frontonasal dysplasia) AND (dysmorphogenesis OR abnormal

Cranial-facial

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Double-click on cell to run query

... And an easy way to query!

Landscape sheet – build from blank

	A	B	C	E	F	G	H
1	Abstract Sifter	Landscape View					
2			<div>Update Article Counts</div> <div>View / hide queriesHeat Map by columnHeat Map by row</div>				
3							
4							
5	DSSTOX link to Dashboard	Preferred Name	Chemical / Entity query				
6							
7							
8							
9							
10							
11							

Select chemical rows and delete

Select subject matter columns and delete

Landscape sheet – build from blank

	A	B	C	E	F
1	Abstract Sifter	Landscape View			
2			<div>Update Article Counts</div> <div>View / hide queries</div> <div>Heat Map by column</div> <div>Heat Map by row</div>		
3					
4					
5	DSSTOX link to Dashboard				
6					
7		DSSTOX link to Dashboard	Preferred Name	Chemical / Entity query	
8					
9					
10					
11		DTXSID50472955	AGN 193109	R 115866 or talarozole	
12		DTXSID0040709	Tributyltin	171568-43-7 OR AGN 193109	
13		DTXSID9020584	Ethanol	688-73-3 OR Tributyltin	
14		DTXSID6024836	3,7-Dimethyl-2,6-octadienal	64-17-5 OR Ethanol	
15		DTXSID1024122	Glyphosate	5392-40-5 OR 3,7-Dimethyl-2,6-octadienal OR citral	
16		DTXSID3020627	Fluconazole	1071-83-6 OR Glyphosate	
17		DTXSID3023897	Triadimefon	86386-73-4 OR Fluconazole	
18		DTXSID0032493	Triadimenol	43121-43-3 OR Triadimefon	
19		DTXSID3024235	Flusilazole	55219-65-3 OR Triadimenol OR triadimefon	
20				85509-19-9 OR Flusilazole	

Enter a chemical name in column C

These columns to Landscape	Mc
71441-28-6 OR Arotinoid acid OR 4-(2TTI	
171568-43-7 OR AGN 193109	
688-73-3 OR Tributyltin	
64-17-5 OR Ethanol	
5392-40-5 OR 3,7-Dimethyl-2,6-octadienal	
1071-83-6 OR Glyphosate	
86386-73-4 OR Fluconazole	
43121-43-3 OR Triadimefon	
55219-65-3 OR Triadimenol OR triadime	
85509-19-9 OR Flusilazole	

Or copy from somewhere ... like the CuratedLists sheet and paste

Landscape sheet – build from blank

Landscape View	
<div>Update Article Counts</div> <div>View / hide queries</div> <div>Heat Map by column</div> <div>Heat Map by row</div>	
Subject queries: toxicity	
Summary heading	
Preferred Name	Chemical / Entity query
	R 115866 or talarozole
AGN 193109	171568-43-7 OR AGN 193109
Tributyltin	688-73-3 OR Tributyltin
Ethanol	64-17-5 OR Ethanol

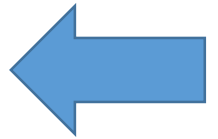
Enter a query term in row 3

Landscape sheet – build from blank

Landscape View							
				Update Article Counts	View / hide queries	Heat Map by column	Heat Map by row

Landscape sheet – build from blank

B	C	E	F	G	H	I
Landscape View	<div>Update Article Counts</div> <div>View / hide queries</div> <div>Heat Map by column</div> <div>Heat Map by row</div>					
			retinoic acid receptor OR retinoic acid receptor gamma OR retinoic Cranial-facial	retinoic acid response element OR gene expression OR retinoic acid signalling Cranial-facial	OR neural crest) AND (patterning OR body patterning) Cranial-facial	palate OR cleft lip OR skull OR jaw OR craniofacial anomaly OR cleft Cranial-facial
		Subject queries: toxicity				
		Summary heading				
Preferred Name	Chemical / Entity query		1mie	2ke	3ke	4ao
AGN 193109	R 115866 or talarozole					
Tributyltin	171568-43-7 OR AGN 193109					
Ethanol	688-73-3 OR Tributyltin					
	64-17-5 OR Ethanol					



Next, select cells and click on Update Article Counts

Landscape sheet – build from blank

Landscape View		E	F	G	H	I
Update Article Counts		View / hide queries		Heat Map by column		Heat Map by row
<p>Article counts are filled in. Select a heat map for color.</p>		Subject queries:		toxicity		
		Summary heading				
Preferred Name	Chemical / Entity query		1mie	2ke	3ke	4ao
	R 115866 or talarozole	0	6	14	0	1
AGN 193109	171568-43-7 OR AGN 193109	6	30	16	0	2
Tributyltin	688-73-3 OR Tributyltin	989	3	200	0	7
Ethanol	64-17-5 OR Ethanol	14403	14	8085	2	204
3,7-Dimethyl-2,6-octadienal	5392-40-5 OR 3,7-Dimethyl-2,6-octadienal OR citral					

Time for questions and trying it out ...
