



Literature Mining Methods for Toxicology and Construction of Adverse Outcome Pathways

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Text mining – why do it?

Unstructured
Text



Structured
data

Abstract
Dose-response of the teratogenic effect of caffeine (CA) and the potential role of facial hematomas in the pathogenesis of caffeine-induced cleft palate were investigated using CD1 mice treated with 150, 200, or 250 mg/kg CA i.p. on gestational day (GD) 12. Dimethylsulfoxide (DMSO, 20%) and arachidonic acid (AA, 200 mg/kg) were administered along with CA (200 mg/kg) to study their interaction with CA-induced teratogenesis and elevation in maternal glucocorticoids (MGC, measured by RIA) on GD 13 and 14. Dose-dependent increase in the incidence of cleft palate (CP) was noted in CA-exposed mice. High maternal deaths, an increased number of resorptions, gross facial hematomas (GFH), and club foot (CF) were produced only by the highest (250 mg/kg) dose of CA. Palates from all offspring with GFH were clefted at this dose level. None of the control or CA-treated nonclefted offspring had GFH or microscopic hematomas (MH). At 200 mg/kg of CA, DMSO in combination with CA actually increased CA-induced CP from 30% to 100% and also produced 100% GFH as compared to 0% by CA alone at this dose. Greater than 50% of clefted offspring without GFH given either dose (200 or 250 mg/kg) of CA, had MH. Very high levels of MGC were present in CA-treated mice on GD 13 and 14. Although simultaneous administration of DMSO reduced the magnitude of CA-induced MGC elevations on GD 14, the MGC levels remained high to greater than 24 hours following CA exposure. Increase in maternal mortality and fetal resorptions, a decrease in the number of live pups and their body weights, and no change in the incidence of CP were seen when CA-treated mice were simultaneously exposed to AA. These results suggest a correlation between caffeine-induced FH and CP, a role for increased hematopoietic effects of DMSO in its potentiation of the cleft-palatogenic effect of caffeine, and absence of a role for AA-mediated effects of MGC in the causation of CA-induced CP and other malformations.

1 and 100-fold or more levels, as well as significant decrease in corticosteroid levels, were observed; no significant difference in corticosteroid transcript level is observed with progressive development. In CORT-exposed palates, we demonstrate no significant differences in the direction or magnitude of change with time in TGF-beta 1, TGF-beta 3, and EGF-R mRNA levels compared to controls. However, CORT delays by 1 day the down-regulation of palatal TGF-beta 2 transcript normally seen on day 14 of gestation. TGF-beta 2 is known to inhibit cell proliferation. The level of TGF-beta 2 transcript in the palate is known to be important for palatal development.

Coumarin is the basic structure of numerous naturally occurring compounds with important and diverse physiological activities. More than a thousand coumarin derivatives have been described, varying from simple coumarins containing alkyl and hydroxyl side chains to complex coumarins with benzoyl, furanoyl, pyranoyl, or alkylphosphonate substituents. Coumarin and 3,4-dihydrocoumarin were monitored by the Food and Drug Administration and the National Cancer Institute for study because of the widespread use of coumarin in perfumes, cosmetics, and other products as a fragrance, perfumed ingredients in cosmetics, and as flavor-enhancing agents for foods, and the interest in its structure-activity relationships in this important group of compounds. Coumarin is believed to be metabolized to a 3,4-epoxide intermediate, which may be responsible for its toxic effects, while 3,4-dihydrocoumarin, which lacks the 3,4-double bond, is not considered likely to form an epoxide intermediate. Toxicity and carcinogenicity studies were conducted by administering coumarin (97% pure) in corn oil by gavage to groups of male and female F344/N rats and B6C3F1 mice for 15 days, 10 weeks, and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*, cultured Chinese hamster ovary cells, *Crotophaga melanogaster*, and B6C3F1 mice. 15-DAY STUDY IN RATS: Groups of five male and five female rats received coumarin in corn oil by gavage at doses of 0, 25, 50, 100, 200, or 400 mg per kg body weight, 5 days a week for a total of 12 doses in a 16-day period. All female rats and four male rats receiving 400 mg/kg died. The mean body weight gains and final mean body weights of surviving dosed male and female rats were similar to those of the controls. There were no clinical signs of organ-specific toxicity, and there was no evidence of impaired blood coagulation from measurements of capillary clotting time or prothrombin and activated partial thromboplastin time. 15-DAY STUDY IN MICE: Groups of five male and five female mice received coumarin in corn oil by gavage at doses of 0, 40, 75, 150, 300, or 500 mg per kg body weight, 5 days a week for a total of 12 doses in a 16-day period. All mice receiving 500 mg/kg, two male mice receiving 300 mg/kg, and one male mouse receiving 75 mg/kg died. The mean body weight gains and final mean body weights of surviving dosed male and female mice were similar to those of the controls. Clinical findings of ataxia, excessive lacrimation, prostration, blepharitis, ptosis, or ataxia were observed in some mice from the 500 and 600 mg/kg groups within the first several hours after dosing. Capillary clotting time and platelet counts of dosed mice were similar to those of controls. 13-WEEK STUDY IN RATS: Groups of 10 male and 10 female rats received coumarin in corn oil by gavage at doses of 0, 10, 30, 75, 150, or 300 mg per kg body weight. Three male and three female rats receiving 300 mg/kg died. The mean body weight gains and final mean body weights of male rats that received 150 and 300 mg/kg were significantly lower than those of the controls. There were no clinical signs related to specific organ toxicity. Male and female rats receiving coumarin exhibited dose-related decreases in mean erythrocyte volume and mean erythrocyte hemoglobin, and dose-related increases in erythrocyte counts. Serum levels of total bilirubin and one or more cytoplasmic enzymes including aspartate aminotransferase, aspartate aminotransferase, ornithine carbonyltransferase, and/or sorbitol dehydrogenase in males and females receiving 300 mg/kg were higher than those of controls. The absolute and relative liver weights of male and female rats that received 150 and 300 mg/kg were significantly greater than those of the controls. Contributary hepatocellular degeneration and necrosis, chronic active inflammation, and bile duct hyperplasia were observed in the liver of rats receiving 150 or 300 mg/kg. The high dose selected for the 2-year study was 100 mg/kg, which was just below the level at which mortality, lower final mean body weights, and treatment-related liver lesions were observed in the 15-week study. 13-WEEK STUDY IN MICE: Groups of 10 male and 10 female mice received coumarin in corn oil by gavage at doses of 0, 10, 30, 75, 150, or 300 mg per kg body weight. Two male mice receiving 300 mg/kg died. The mean body weight gains and final mean body weights of surviving

Chemical	Gene	Amount
Corticosterone	NR3C1	416
Tretinoin	RARA	397
Mifepristone	NR3C1	260
Fenofibrate	PPARA	189
Estradiol	EGFR	119
Tretinoin	RARG	111
Tamoxifen	EGFR	96
Tretinoin	EGFR	86
Triamcinolone	NR3C1	83
Lovastatin	LDLR	65
Estradiol	NR3C1	60
Estradiol	MMP9	54
Genistein	EGFR	50
Phenobarbital	NR1I3	48

- Integrate
- Analyze
- Cluster
- Model
- Infer
- Visualize
- Discover
- Deal with Error / noise / bias

Anatomy of a PubMed record

The screenshot shows a web browser window with the address bar displaying a search for "chlorpyrifos AND cleft palate". The browser's address bar shows the URL: `ed/?term=chlorpyrifos+AND+cleft+palate`. The browser's address bar also shows the search term: "chlorpyrifos AND cleft palate". The browser's address bar also shows the search term: "chlorpyrifos AND cleft palate".

Abstract Send to: ▾

Reprod Toxicol. 2005 Jul-Aug;20(2):267-70.

Teratogenicity and developmental toxicity of chlorpyrifos. Maternal exposure during organogenesis in mice.

Tian Y¹, Ishikawa H, Yamauchi T, Yamauchi T, Yokoyama K.

Author information

Abstract

Chlorpyrifos, an organophosphate pesticide, was evaluated for potential teratogenicity and developmental toxicity in mice. Pregnant females were given a single intraperitoneal injection (40 or 80 mg/kg) on day 10 of gestation and fetuses were evaluated on gestation day 17. At 80 mg/kg, chlorpyrifos treatment resulted in a significant reduction in numbers of live fetuses, and increase in resorptions, versus control litters. There was no indication of maternal toxicity. External and skeletal malformations were observed at 80 mg/kg, but not 40 mg/kg. Rates of fetuses with cleft palate increased significantly ($p < 0.05$) following 80 mg/kg chlorpyrifos (5.97%) versus control litters (0.97%). Similarly, the absence of thoracic vertebrae was increased and the number of caudal vertebrae was significantly decreased. It is suggested that chlorpyrifos is teratogenic and embryotoxic in mice at doses below those that cause significant maternal toxicity.

PMID: 15907662 [PubMed - indexed for MEDLINE]

MeSH Terms, Substances ▾

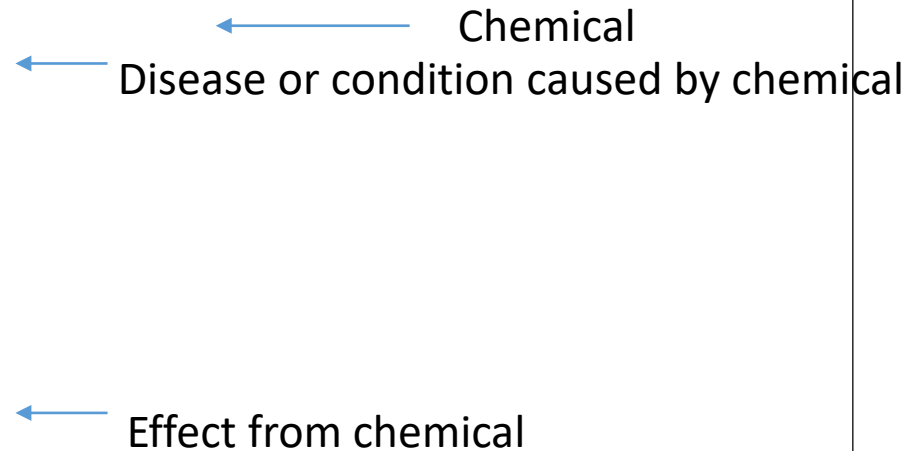
LinkOut - more resources ▾

MeSH
Indexing
annotations

MeSH

- **M**edical **S**ubject **H**eadings
- Not designed to be used as data ... but that's what many people do.
- But like data they are a controlled vocabulary

Format: Heading / subheading



Indexing terms → data

PubMed ID	MeSH heading	Qualifier / subheading	Majr
15907662	Chlorpyrifos	Administration & dosage	N
15907662	Chlorpyrifos	Toxicity	Y
15907662	Cleft Palate	Chemically induced	N
15907662	Fetal resorption	Chemically induced	N
15907662	Hernia, abdominal	Chemically induced	N
15907662	Neural tube defects	Chemically induced	N
15907662	Organogenesis	Drug effects	Y
15907662	Polydactyly	Chemically induced	N
15907662	Spine	Drug effects	N
15907662	Mice		

High-throughput text-mining: a few readouts per article, but it adds up ...

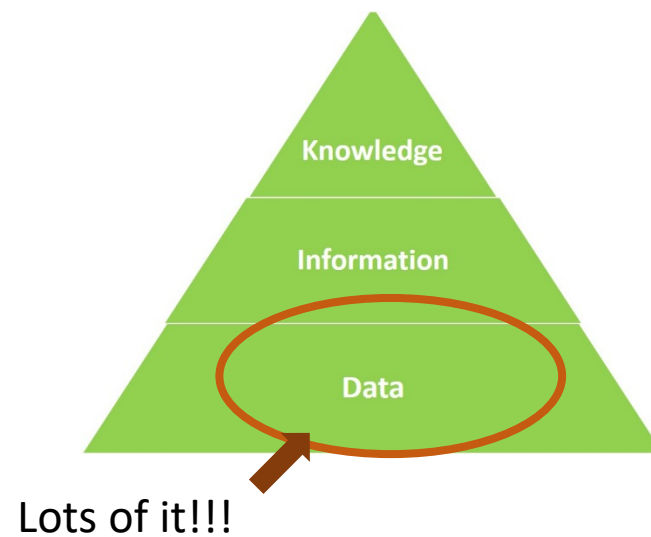
Chlorpyrifos – 2174 articles

Disease List		
Chemical	Disease/condition	PMID Count
Chlorpyrifos	Behavior, Animal	84
Chlorpyrifos	Motor Activity	60
Chlorpyrifos	Body Weight	42
Chlorpyrifos	Maze Learning	21
Chlorpyrifos	Cognition	14
Chlorpyrifos	Nervous System Diseases	13
Chlorpyrifos	Prenatal Exposure Delayed Effects	12
Chlorpyrifos	Memory	11
Chlorpyrifos	Reaction Time	10
Chlorpyrifos	Peripheral Nervous System Diseases	10
Chlorpyrifos	Psychomotor Performance	8
Chlorpyrifos	Occupational Diseases	7
Chlorpyrifos	Cognition Disorders	7
Chlorpyrifos	Agricultural Workers' Diseases	7
Chlorpyrifos	Hypothermia	7
Chlorpyrifos	Learning	7
Chlorpyrifos	Cat Diseases	6
Chlorpyrifos	Weight Gain	6
Chlorpyrifos	Reflex, Startle	5
Chlorpyrifos	Space Perception	5
Chlorpyrifos	Memory, Short-Term	5
Chlorpyrifos	Cattle Diseases	5
Chlorpyrifos	Fever	5
Chlorpyrifos	Feeding Behavior	5
Chlorpyrifos	Attention	4
Chlorpyrifos	Avoidance Learning	4
Chlorpyrifos	Memory Disorders	4
Chlorpyrifos	Impulsive Behavior	4
Chlorpyrifos	Visual Perception	4

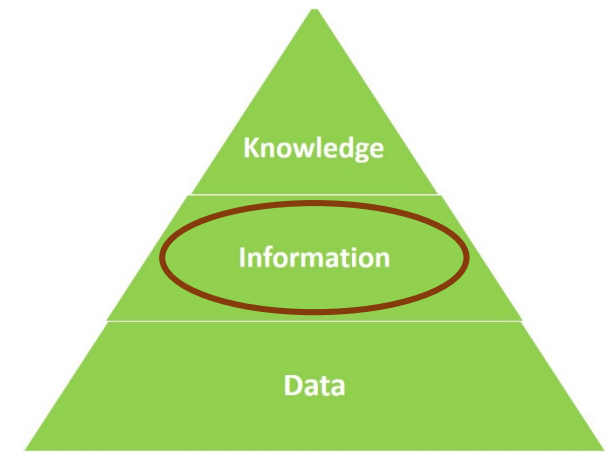
Protein / gene List	
Protein / gene	PMID Count
Acetylcholinesterase	488
Cholinesterases	465
Receptors, Muscarinic	57
Esterases	47
Aryldialkylphosphatase	47
Cytochrome P-450 Enzyme System	42
Glutathione Transferase	37
Carboxylesterase	35
Carboxylic Ester Hydrolases	35
Butyrylcholinesterase	33
Superoxide Dismutase	30
Catalase	29
Glutathione	24
Enzymes	23
Receptors, Nicotinic	19
Recombinant Proteins	19
Isoenzymes	17
Glutathione Peroxidase	16
Nerve Tissue Proteins	16
Choline O-Acetyltransferase	15
PON1 protein, human	15
Adenylate Cyclase	15
Enzymes, Immobilized	13
neurotoxic esterase	13
Oxidoreductases	13
Cytochrome P-450 CYP3A	12
L-Lactate Dehydrogenase	12
Glycine	12
glyphosate	12
Membrane Transport Proteins	10
CYP3A4 protein, human	10
Proteins	10
Receptors, Cholinergic	10

The numbers (approximately)

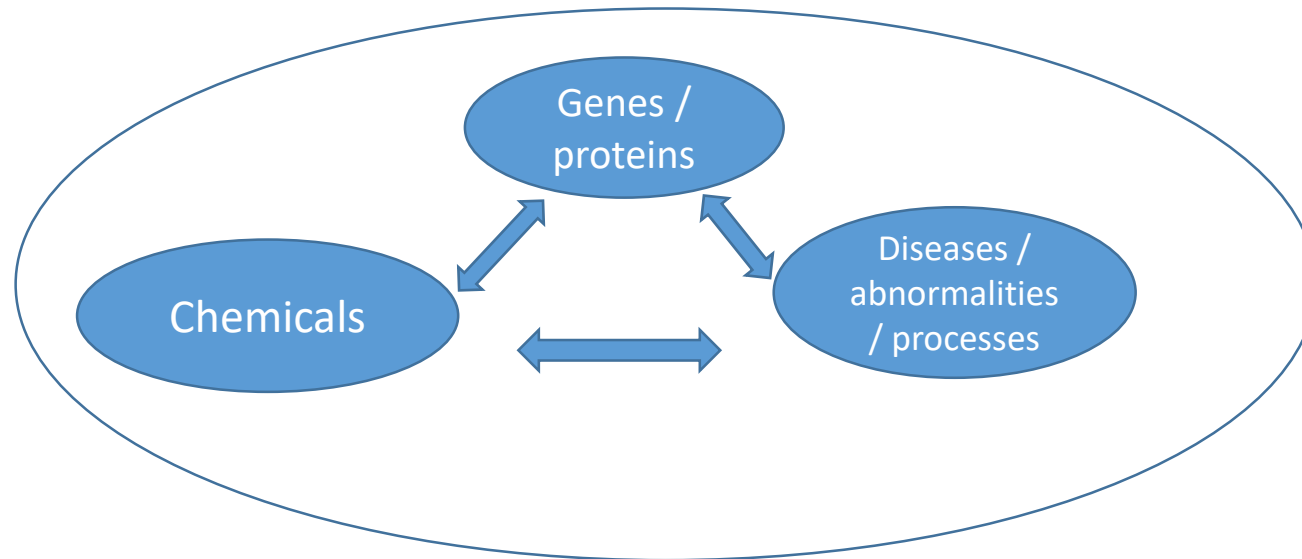
- 24 million articles in PubMed
- 12 million articles have chemical annotations
- 190 million MeSH annotations
- 12 million annotations are my additions
- Growth
 - 1 million annotations / month
 - More next year



So we have lots of data ... what can we do with it?



- Delivery forms
 - Dashboard – for basic information delivery
 - E-libraries – for very specific computationally intensive problems



And in what context:

- Species
- Life stage

Relationship: chemical – protein

	A	B	Z	AA	AB	AC	AD	AE	AH	AI	AV	AW	BX	CC	CD	CK	CL
1	Overview																
2																	
		ToxCast?	Estrogen Receptor alpha	Estrogen Receptor alpha	Estrogen Receptor beta	Estrogen Receptor beta	farnesoid X-activated receptor	farnesoid X-activated receptor	Iodide Peroxidase	Lactoperoxidase	Peroxisome Proliferator-Activated Receptors	Peroxisome Proliferator-Activated Receptors	Receptors, Androgen	Receptors, Estrogen	Receptors, Estrogen	Receptors, Retinoic Acid	Receptors, Retinoic Acid
3	Chemical																
4	Tretinoin	1	0	0	0	0	0	0	0	0	0	0	0	0	1	77	82
5	alitretinoin	1	0	0	0	0	0	0	0	0	0	0	0	0	0	14	8
6	rosiglitazone	1	0	0	0	0	2	0	0	0	13	1	0	0	0	12	2
7	bexarotene	1	0	0	0	1	0	0	0	0	0	0	0	0	0	11	3
8	tamibarotene	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11	0
9	Am 580	1	0	0	0	0	0	0	0	0	0	0	0	0	0	10	3
10	LG 100268	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	2

1	Article List						
2	Target\Activity	Chemical	TC	PMID	Pub Yr	Title	
8442	Receptors, Retinoic Acid	AGN 194204	0	11428923	2001	Enantioselective syntheses of potent retinoid X receptor ligands: differential biological activities o	
8443	Receptors, Retinoic Acid	AGN 194204	0	14712350	2004	Retinoic acid receptor alpha and retinoid X receptor specific agonists reduce renal injury in establis	
8444	Receptors, Retinoic Acid	AGN 195183	0	14712350	2004	Retinoic acid receptor alpha and retinoid X receptor specific agonists reduce renal injury in establis	
8445	Receptors, Retinoic Acid	alitretinoin	1	11397803	2001	Regulation of stearyl coenzyme A desaturase expression in human retinal pigment epithelial cell	
8446	Receptors, Retinoic Acid	alitretinoin	1	11261782	2001	Retinoic acid up-regulates myeloid ICAM-3 expression and function in a cell-specific fashion--evid	
8447	Receptors, Retinoic Acid	alitretinoin	1	12006550	2002	Nuclear receptor agonists as potential differentiation therapy agents for human osteosarcoma.	
8448	Receptors, Retinoic Acid	alitretinoin	1	12882839	2003	Retinoic acids exert direct effects on T cells to suppress Th1 development and enhance Th2 develo	
21	AGN 190121		0	0	0	0	2
22	AGN 194204		0	0	0	0	2
23	ALRT 1550		0	0	0	0	2
24	Calcitriol		0	0	0	0	2
25	CD 2019		0	0	0	0	2
26	ciglitazone		0	0	0	0	3
27	ER 34617		0	0	0	0	2
28	LG 100754		0	0	0	0	2
29	Iuffariellolide		0	0	0	0	2
30	octa-2,4,6-trienoic acid		0	0	0	0	2
31	Palovarotene		0	0	0	0	2

Relationship: chemical – disease or condition

[illegible]

Examples

[illegible]

Disease and protein

1	Proteins annotated with hypospadias			
2	Protein	PMID	PubYr	Title
3	17beta-hydroxysteroid dehydrogenase type 3	20059664	2010	Genetic polymorphisms of 17 β -hydroxysteroid dehydrogenase 3 and the risk of hypospadias.
4	17-Hydroxysteroid Dehydrogenases	6332300	1984	An improved method for evaluating testosterone biosynthetic defects.
5	17-Hydroxysteroid Dehydrogenases	6105737	1980	Pseudovaginal perineoscrotal hypospadias: genetic heterogeneity.
6	17-Hydroxysteroid Dehydrogenases	20059664	2010	Genetic polymorphisms of 17 β -hydroxysteroid dehydrogenase 3 and the risk of hypospadias.
7	17-Hydroxysteroid Dehydrogenases	9112555	1997	Defects of the testosterone biosynthetic pathway in boys with hypospadias.
8	20-Hydroxysteroid Dehydrogenases	3160950	1985	Elevated 17-hydroxyprogesterone and testosterone in a newborn with 3-beta-hydroxysteroid dehydrogenase deficiency.
9	3 (or 17)-beta-hydroxysteroid dehydrogenase	9112555	1997	Defects of the testosterone biosynthetic pathway in boys with hypospadias.
10	3-Hydroxysteroid Dehydrogenases	15181062	2004	Lack of defects in androgen production in children with hypospadias.
11	3-Hydroxysteroid Dehydrogenases	14764821	2004	Molecular study of the 3 beta-hydroxysteroid dehydrogenase gene type II in patients with hypospadias.
12	3-Hydroxysteroid Dehydrogenases	6603965	1983	Differences in inhibition by various steroids of rat testis and Pseudomonas testosteroni delta 5-3 beta-hydroxysteroid dehydrogenase.
13	3-Hydroxysteroid Dehydrogenases	3867211	1985	Male pseudohermaphroditism due to 3 beta-hydroxysteroid dehydrogenase-isomerase deficiency associated with atrial septal defect.
14	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	8723114	1996	Phenotypic classification of male pseudohermaphroditism due to steroid 5 alpha-reductase 2 deficiency.
15	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	1568634	1992	[A case of pseudo-vaginal, perineoscrotal hypospadias with 5-alpha reductase deficiency].
16	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	512549	1979	Reduction of androstenedione by skin in vitro and serum levels of gonadotrophins and androgens in men with hypospadias.
17	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	17609295	2008	Molecular characterization of 6 unrelated Italian patients with 5alpha-reductase type 2 deficiency.
18	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	8789759	1996	Molecular genetic analysis and human chorionic gonadotropin stimulation tests in the diagnosis of prepubertal patients with partial 5 alpha-reductase deficiency.
19	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	3920857	1985	Endocrine and immunogenetic evaluation of an XX male infant with perineoscrotal hypospadias.
20	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	564935	1978	Metabolism of androstenedione in skin and serum levels of gonadotrophins and androgens in prepubertal boys with hypospadias.
21	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	22678668	2012	Environmental and genetic contributors to hypospadias: a review of the epidemiologic evidence.
22	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	8339743	1993	The androgen resistance syndromes: clinical and biochemical aspects.
23	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	18097518	2008	Molecular diagnosis of 5alpha-reductase-2 gene mutation in two Indian families with male pseudohermaphroditism.
24	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	2913055	1989	Intracellular and nuclear binding of [3H]dihydrotestosterone in cultured genital skin fibroblasts of patients with severe hypospadias.
25	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	6105737	1980	Pseudovaginal perineoscrotal hypospadias: genetic heterogeneity.
26	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	521711	1979	Further studies of testosterone 5 alpha-reductase deficiency in human fibroblasts [proceedings].
27	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	16736621	2006	[Mutation analysis of SRD5A2 gene in patients with hypospadias].
28	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	3263511	1988	Androgen receptor levels and 5 alpha-reductase activities in preputial skin and chordee tissue of boys with isolated hypospadias.
29	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	6699962	1984	Endocrine studies in patients with advanced hypospadias.
30	3-Oxo-5-alpha-Steroid 4-Dehydrogenase	6480803	1984	Partial androgen resistance associated with secondary 5 alpha-reductase deficiency: identification of a novel qualitative androgen receptor defect.

Literature signal at a high level over several toxicity types

	A	B	C	J	K	L	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL
1	Overview																											
2																												
3				DevTox		Obesity				ReproTox				Thyroid														
				Abnormality	Embryonic Structures	Morphogenesis	Adipogenesis	Adipose Tissue	Clinical Conditions	Proteins and genes	Abnormality	Cancer	FemaleRepro	Infertility	MaleRepro	Processes	Binding Proteins	Hormones	Receptors	Synthesis	Hepatic Catabolism	TR Contolled Genes	Transporters	Body Temp Reg.	Clinical Conditions	Cognition_IQ	Frog	Thyroid Gland
5	Chemical	gsid	cas																									
6	Diethylhexyl Phthalate	20607	117-81-7	79	55	51	5	8	97	11	9	11	79	20	268	407	1	18	2	2	19	1	0	0	0	7	0	5
7	Diethylstilbestrol	40770	6898-97-1	357	209	72	0	0	63	1	36	95	632	74	255	1216	8	70	0	24	8	0	0	3	0	3	0	4
8	Cyclophosphamide	208761	60030-72-0	390	185	101	0	1	113	1	0	45	150	88	234	513	0	36	0	10	6	10	1	4	7	26	0	6
9	bisphenol A	27480	2444-90-8	69	125	146	2	21	184	36	3	0	184	36	200	809	0	60	19	7	40	4	1	0	0	27	30	11
10	Dibutyl Phthalate	21781	84-74-2	111	33	45	0	0	32	3	21	3	22	12	194	212	0	5	6	1	2	0	0	0	3	1	4	0
11	Estradiol	20573	50-28-2	89	57	60	0	3	96	182	12	7	296	24	149	792	43	762	22	129	115	42	21	0	0	19	16	7
12	Ethinyl Estradiol	20576	57-63-6	103	47	87	0	3	149	9	0	4	232	8	107	799	14	66	0	6	19	0	3	1	0	7	26	6
13	Flutamide	32004	13311-84-7	63	1	13	0	2	18	5	15	0	12	4	91	77	0	3	0	0	4	3	1	0	0	0	0	1
14	methyl cellosolve	24182	109-86-4	85	31	27	0	0	34	0	0	0	15	4	87	141	0	0	0	1	1	0	0	2	0	0	0	0
15	mono-(2-ethylhexyl)phthalate	25680	4376-20-9	5	16	7	2	2	7	2	0	3	19	0	75	24	0	3	0	0	6	0	0	0	0	0	0	1
16	Atrazine	20112	1912-24-9	73	25	121	0	2	45	0	3	0	58	0	70	207	0	14	0	3	0	0	0	1	3	8	133	7
17	vinclozolin	22361	50471-44-8	32	9	36	0	0	15	0	12	0	10	12	69	156	0	5	0	0	0	1	0	2	0	0	0	1
18	3-dinitrobenzene	24065	99-65-0	0	0	0	0	0	5	0	0	0	2	8	66	12	0	0	0	0	0	0	0	0	0	0	0	0
19	tributyltin	40709	688-73-3	162	35	67	4	16	46	8	0	0	31	0	66	174	0	6	2	1	3	0	0	0	0	1	10	2
20	Testosterone	22371	58-22-0	38	7	11	0	1	19	52	2	0	41	8	63	96	9	301	6	10	28	2	0	2	2	0	0	4
21	carbendazim	58370	37574-18-8	9	14	8	0	0	12	0	0	0	7	4	59	56	0	5	0	1	0	0	0	0	0	0	0	1
22	Lindane	20686	58-89-9	24	30	28	0	16	50	0	0	0	31	12	58	192	0	20	0	5	2	0	0	7	5	8	0	7
23	Methotrexate	20822	59-05-2	293	35	44	2	1	91	5	0	27	45	20	55	427	1	7	0	5	13	12	33	3	2	154	0	3
24	Carbendazim	58370	37574-18-8	9	14	8	0	0	12	0	0	0	7	4	59	56	0	5	0	1	0	0	0	0	0	0	0	1

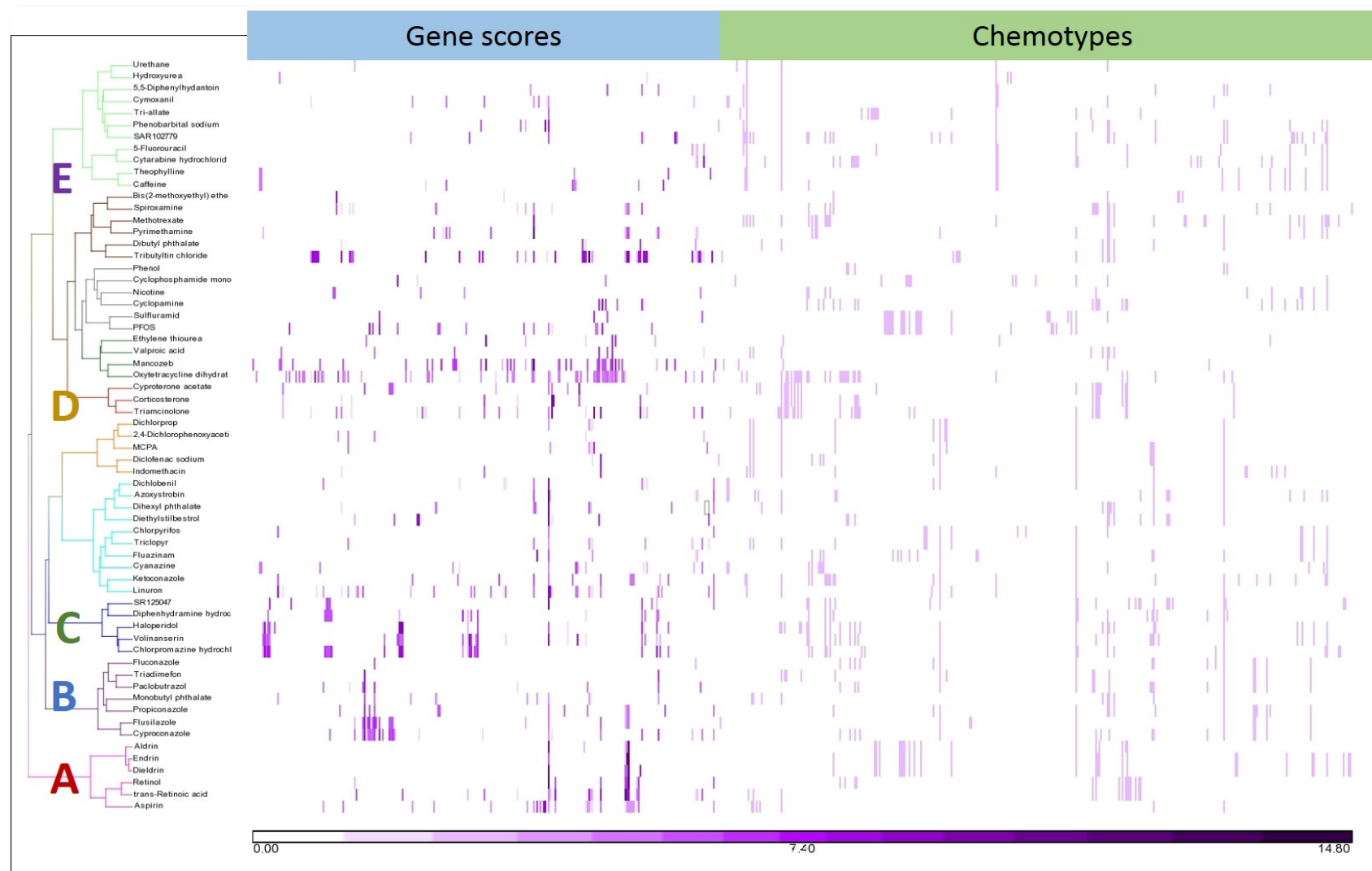
Integration: ToxCast and literature

	A	D	F	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
1	Overview																															
2				Scores (annotation count * arbitrary weights)																												
3		ATG_Ahr_CIS_up		DevTox		GeneTox		Obesity		ReproTox					Thyroid																	
		AC50	Hit Call	Abnormality	Anbryonic Structures	Morphogenesis	Mutagen	RNA Damage/Repair	Genetic Structures	Processes	Adipogenesis	Adipose Tissue	Clinical Conditions	Proteins and genes	Abnormality	Cancer	FemaleRepro	Infertility	MaleRepro	Processes	Binding Proteins	Hormones	Receptors	Synthesis	Hepatic Catabolism	TR Contolled Genes	Transporters	Body Temp Reg.	Clinical Conditions	Cognition_IQ	Frog	Thyroid Gland
5	Chemical																															
86	1-phenylazo-2-naphthol	-1.418118069	1	0	0	0	12	24	8	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0
97	Acetaldehyde	-1.252319017	1	1	4	2	24	12	9	0	0	0	2	0	0	0	1	0	4	5	0	2	0	0	0	0	0	1	0	0	0	0
102	1,2,5,6-dibenzanthracene	-1.21708267	1	0	0	0	6	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
138	indole-3-carbinol	-1.031070118	1	0	0	0	9	6	8	0	0	0	4	0	0	0	0	0	3	1	0	0	0	0	0	0	0	0	0	0	0	2
147	Apomorphine	-0.625806458	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	5	0	0	4	0	0	0	0	0	0	0	0
150	benz(a)anthracene	-0.390970114	1	0	0	4	15	18	21	0	0	0	1	0	0	3	3	0	1	4	0	3	0	0	1	0	0	0	0	0	0	0
287	4-chloro-1,2-diaminobenzene	-0.372897034	1	0	0	0	12	3	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
292	indeno(1,2,3-cd)pyrene	-0.289718708	1	0	0	0	3	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
293	Ketoconazole	-0.193907372	1	28	3	5	0	0	5	1	0	1	2	0	0	0	8	0	18	29	0	18	0	2	20	0	3	0	5	4	0	1
300	1,4-naphthoquinone	-0.192036977	1	0	1	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
304	beta-Naphthoflavone	-0.189962165	1	0	1	0	3	27	1	0	0	0	0	0	0	0	1	0	0	2	0	1	0	0	6	0	0	0	0	0	0	0
332	Cycloheximide	-0.124700601	1	4	4	1	30	24	183	2	0	0	0	0	0	0	1	0	0	8	0	43	7	12	0	0	0	0	0	4	2	0
353	3,3',5,5'-tetramethylbenzidine	-0.112828864	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0
377	Methenamine	-0.064371953	1	0	1	0	12	3	2	0	0	0	2	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0
430	dibenzo(1,4)dioxin	-0.058282855	1	1	0	0	0	0	0	0	0	2	1	0	0	0	0	0	0	1	0	2	0	0	0	0	0	0	0	0	0	1

Integration: ToxCast and chemical structure as chemotypes

In this figure: chemicals that cause cleft palate and have ToxCast results in the form of gene scores (summarized by gene and burst-adjusted)

The chemicals were clustered based on their ToxCast scores and structure. The hypothesis: chemicals that cluster together cause cleft palate through a similar mechanism.



Summary

- Literature mining can be used to investigate the retinoid system on several levels from several angles
- Integration possible
 - ToxCast and literature
 - ToxCast and chemical structure

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