

T3DB - The Toxin, Toxin-Target Database

David Wishart david.wishart@ualberta.ca

University of Alberta, Edmonton, AB, Canada

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**Communities of Practice – US EPA
National Center for Computational Toxicology**

Outline

- **Brief review of toxicology databases**
- **Metabolomics and toxicology**
- **Introducing the toxin, toxin-target database – T3DB**
- **Systems biology, pathway databases and the small molecule database - SMPDB**
- **Conclusions & Future Directions**

Toxicology Databases

www.epa.gov/actor/

<http://bioinf-services.charite.de/supertoxic/>

www.ctdbase.org

<http://toxnet.nlm.nih.gov/>

ACToR Database

The image displays three overlapping screenshots of the ACToR database website. The top screenshot shows the home page with the EPA logo and navigation links. The middle screenshot shows a detailed entry for Paraquat, including its chemical structure, CASRN (4685-14-7), and a description. The bottom screenshot shows search results for Paraquat, listing its CASRN (1510-42-5), preferred name (Paraquat dichloride), and various toxicity ratings (Ha, Cr, Ca, G, D, R, FS).

Chemical: Paraquat
PDF Version
Email link to this page: <http://actor.epa.gov/actor/GeneralChemical.aspx#4685-14-7>

OCID: 153974
MESH DESCRIPTION: A poisonous dipyrilium compound used as contact herbicide. Contact with concentrated solutions causes irritation of the skin, cracking and shedding of the nails, and delayed healing of cuts and wounds.; Herbicides
CASRN: 4685-14-7
FORMULA: C12H14N2Cl2
MW: 306.253

Search Results

Details	Image	CASRN	Preferred Name	Chronic Hazard	Toxicity	Carcinogenicity/Genotoxicity	Developmental Toxicity	Reproductive Toxicity	Food Safety	Exposure
details		1510-42-5	Paraquat dichloride	Ha	Cr	Ca	G	D	R	FS
details		4685-14-7	Paraquat	Ha	Cr	Ca	G	D	R	FS
details		2074-00-2	1,1-Dimethyl-4,4'-bipyridinium bis(methyl sulfate)	Ha	Cr		G		R	FS

- Maintained by the EPA Computational Toxicology Program
- Aggregate of 500 public resources
- >500,000 compounds
- Data includes chemical structure, physico-chemical values, in vitro assay data and in vivo toxicology data
- Limited target, action or mechanistic data

SuperToxic Database

The image displays three overlapping screenshots of the SuperToxic database interface. The top screenshot shows the 'HOME' page with a navigation menu on the left and a central text area. The middle screenshot shows the 'RESULTS' page for a 'PROPERTY SEARCH' with a table of chemical compounds and their structures. The bottom screenshot shows the 'Information' and 'Structure' tabs for a specific compound, displaying a list of synonyms and a chemical structure diagram.

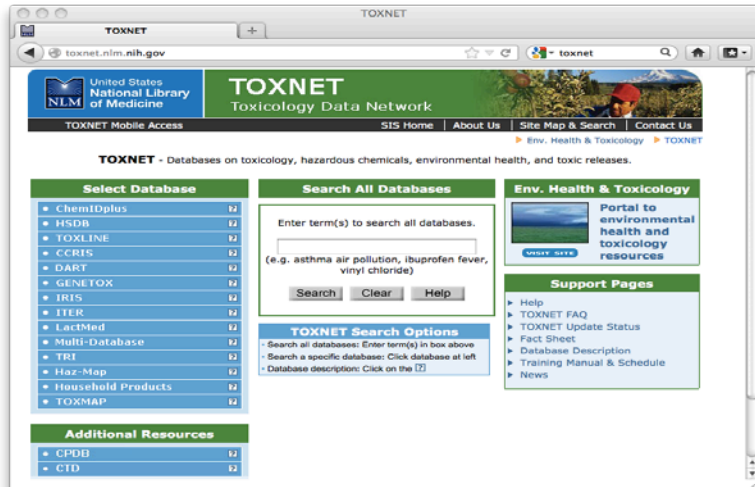
- Maintained by Charite Berlin (Structural Bioinformatics)
- >60,000 compounds, 2,500,000 toxicity measurements
- Data includes chemical structure, physico-chemical values and LC50 data
- No target, no action or mechanistic (MOA) data
- Not updated since 2008

Comparative Toxicogenomics Database

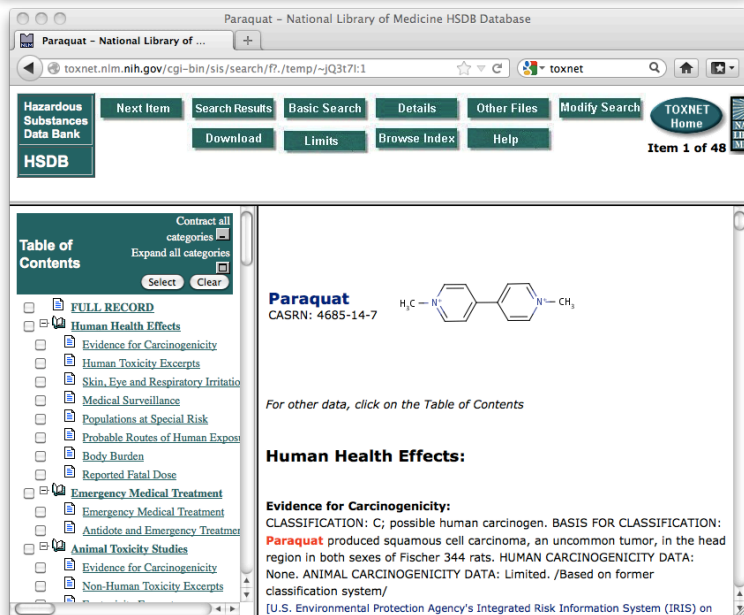
The image displays three overlapping screenshots of the Comparative Toxicogenomics Database (CTD) website. The top screenshot shows the homepage with navigation tabs (Home, Search, Analyze, Download, Help) and a search bar. The middle screenshot shows the details for the chemical Paraquat, including its CAS Registry Number (4685-14-7), a definition, and a bar chart of top interacting genes (RAT, SOD1, SOD2, CASP3, GSK3). The bottom screenshot shows a list of 21 interactions between Paraquat and various genes/proteins, such as AAT-B, AATS-ASB, and AATS-GLUFRO.

- Maintained by Mount Desert Island Biological Lab
- 11,755 compounds, 599,000 chemical-gene associations, 176,000 chemical-disease associations, 23,000 gene-disease assoc.
- Data mostly *from automated text mining*
- No target or MOA data, no context

ToxNet Database



The screenshot shows the ToxNet homepage. At the top, it features the United States National Library of Medicine (NLM) logo and the ToxNet Toxicology Data Network banner. Below the banner, there are navigation links for 'TOXNET Mobile Access', 'SIS Home', 'About Us', 'Site Map & Search', and 'Contact Us'. The main content area is divided into several sections: 'Select Database' with a list of databases like ChemIDplus, HSDB, TOXLINE, etc.; 'Search All Databases' with a search box and buttons for 'Search', 'Clear', and 'Help'; 'Env. Health & Toxicology' with a 'Portal to environmental health and toxicology resources' link; and 'Additional Resources' with links to CPDB and CTD.



The screenshot shows the Paraquat entry in the HSDB database. The page title is 'Paraquat - National Library of Medicine HSDB Database'. The URL is 'toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~jQ3t7:1'. The page has a navigation bar with buttons for 'Next Item', 'Search Results', 'Basic Search', 'Details', 'Other Files', 'Modify Search', 'Download', 'Limits', 'Browse Index', and 'Help'. The main content area includes a 'Table of Contents' on the left with a tree view of categories like 'FULL RECORD', 'Human Health Effects', 'Evidence for Carcinogenicity', etc. The main text area contains the chemical structure of Paraquat, its CASRN (4685-14-7), and a section titled 'Human Health Effects' with a sub-section 'Evidence for Carcinogenicity'.

Paraquat
CASRN: 4685-14-7

CN1C=CC=C1C2=CC=CC=C2N3C

Human Health Effects:

Evidence for Carcinogenicity:
CLASSIFICATION: C; possible human carcinogen. BASIS FOR CLASSIFICATION: **Paraquat** produced squamous cell carcinoma, an uncommon tumor, in the head region in both sexes of Fischer 344 rats. HUMAN CARCINOGENICITY DATA: None. ANIMAL CARCINOGENICITY DATA: Limited. /Based on former classification system/
[U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on

- Maintained by NIH and NLM
- Amalgamation of 15+ different databases on toxicology, hazardous chemicals, environmental health, and toxic releases
- Structure, toxicity, case reports, signs and symptoms
- No target, action or mechanistic data

Toxicology Databases

- **General preference for breadth (lots of compounds) over depth (lots of information)**
- **Most focus on toxicity, not toxicology or molecular mechanisms**
- **Information content is fragmented, appears in multiple formats, difficult to read, limited search utilities, not linked to other resources and sometimes lightly referenced**
- **Emerging resources (ToxcastDB, ToxBank Wiki, T3DB) are starting to change this**

ToxCastDB

The screenshot shows the ToxCastDB website interface. The top navigation bar includes the EPA logo and search options. Below the navigation, there are tabs for 'ACTAR', 'ToxCastDB', 'ExpCastDB', and 'DSSTOX'. The main content area features a search form with 'Enter Chemical Name' and 'Match by' options (Exact, Any). Below the search form, there is a 'Chemical' section showing a chemical structure and its properties: SMILES: ClC1=CC(=CC=C1)C(Cl)=C2C=CC(=CC=C2)Cl, Source Name SID: DSSTOX_40307, Source Name CID: DSSTOX_2325, and ACTor: Find in ACTor DB. The 'Data' section contains a table with assay results.

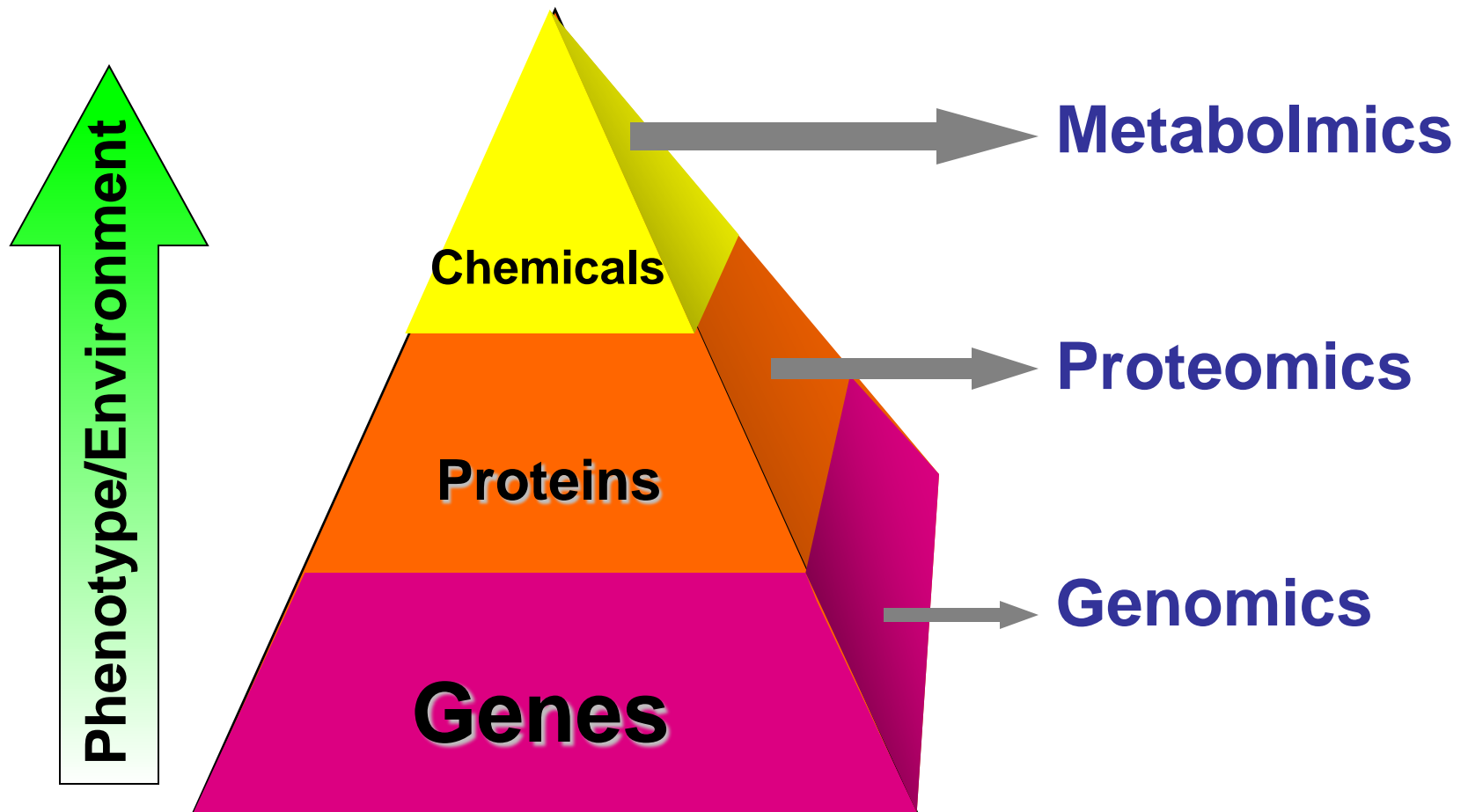
Source	Assay	Assay Name	Species	Gene	Value	Units
ACEA	ACEA_LOCCec	ACEA_LOCCec	Homo sapiens		33.1	uM
ACEA	ACEA_IC50	ACEA_IC50	Homo sapiens		85.8	uM
Attgene	ATO_Era_TRANS	Attgene Factorial trans Era	Homo sapiens	ESR1	0.73	uM
Attgene	ATG_ERK_GIS	Attgene Factorial cis ERK	Homo sapiens	ESR1	0.17	uM
Attgene	ATO_PXRE_CIS	Attgene Factorial cis PXRE	Homo sapiens	NR1H2	0.58	uM
BioSeek	BSK_BE3C_IP10_down	BEP1_IL1b_TNF_a_IPN_a_24_CXCL10_IP_10_down	Homo sapiens	CXCL10	13.3	uM
BioSeek	BSK_BE3C_HADR_down	BEP1_IL1b_TNF_a_IPN_a_24_HLA_DR_down	Homo sapiens	HLA-DRA	13.3	uM
BioSeek	BSK_BE3C_SRB_down	BEP1_IL1b_TNF_a_IPN_a_24_SRB_down	Homo sapiens		40.0	uM
BioSeek	BSK_HDFCGF_VCAM1_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_CD106_VCAM1_down	Homo sapiens	VCAM1	4.44	uM
BioSeek	BSK_HDFCGF_IP10_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_CXCL10_IP_10_down	Homo sapiens	CXCL10	13.3	uM
BioSeek	BSK_HDFCGF_MIG_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_CXCL3_MIG_down	Homo sapiens	CXCL3	13.3	uM
BioSeek	BSK_HDFCGF_CollagenIII_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_CollagenIII_down	Homo sapiens	COL3A1	13.3	uM
BioSeek	BSK_HDFCGF_EGFR_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_EGFR_down	Homo sapiens	EGFR	13.3	uM
BioSeek	BSK_HDFCGF_MCSF_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_M-CSF_down	Homo sapiens	CSF1	13.3	uM
BioSeek	BSK_HDFCGF_PA11_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_PA11_down	Homo sapiens	SERPINE1	13.3	uM
BioSeek	BSK_HDFCGF_Proliferation_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_Proliferation_72hr_down	Homo sapiens		4.44	uM
BioSeek	BSK_HDFCGF_SRB_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_SRB_down	Homo sapiens		40.0	uM
BioSeek	BSK_HDFCGF_TIMP1_down	HDFn_IL1b_TNF_a_IPN_a_EGF_FGF_PDGFb_24_TIMP1_down	Homo sapiens	TIMP1	13.3	uM

- 310 pesticide compounds in Phase I
- 767 drugs, food adds, pesticide compounds in Phase II
- 500+ HTS assays with gene targeting information

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The Pyramid of Life



The Human Metabolome Project



- **\$7.5 million Genome Canada Project launched in Jan. 2005 - Based at the University of Alberta**
- **Key objective was to create a comprehensive database of all human metabolites that included compound data, source data, concentration data and a wide range (NMR, GC-MS, MS/MS) of spectral data**
- **Special focus on metabolites in biofluids such as urine, CSF and blood as well as tissues using HT experiments and text analysis (~40,000 cmpds to date)**
- **Associate metabolite concentrations to ~600 diseases or conditions**
- **Make all data freely and electronically accessible**

Human Metabolomes

2900 (T3DB)

Toxins/Env. Chemicals

2720 (ECMDB)

Microbial metabolites

28500 (FooDB)

Food additives/Phytochemicals

1450 (DrugBank)

Drugs

19700 (HMDB)

Endogenous metabolites



Meet the Metabolomes...

The screenshot shows the HMDB Home page. At the top, there is a navigation menu with 'Home', 'Browse', 'Search', 'About', 'Downloads', and 'Contact Us'. Below this is a search bar with the text 'Search: Search HMDB' and buttons for 'Search' and 'Advanced'. The main heading is 'Human Metabolome Database' with the 'hmp' logo. A paragraph of text describes the database's scope and content. At the bottom, there is a 'What's New?' section with a date 'November 5, 2009' and a list of updates.

<http://www.hmdb.ca>

The screenshot shows the ECMDB Welcome page. It features a blue header with the 'ECMDB' logo and the text 'E. coli Metabolome Database'. Below the header is a navigation menu with 'Home', 'Browse', 'Search', 'About', 'Help', 'Downloads', and 'Contact Us'. A search bar is present with the text 'Search: Search ECMDB' and buttons for 'Search' and 'Advanced Search'. The main content area contains a paragraph describing the database and its manual curation. Below this is a detailed section about search capabilities and a 'What's New?' section.

<http://www.ecmdb.ca>

The screenshot shows the FoodDB Intro page. It has a blue header with the 'FoodDB' logo and the text 'The Food Component Database'. Below the header is a navigation menu with 'Home', 'Browse', 'DrugBank', and 'HMDB'. A search bar is located on the right. The main heading is 'Welcome to the FoodDB food component database!'. A paragraph describes the database's comprehensive information on food components. Below this is a section for questions and corrections, and a list of supported browsers. At the bottom, there is a paragraph about the project's funding and support.

<http://www.foodb.ca>

The screenshot shows the DrugBank website. It features a blue header with the 'DRUGBANK' logo and the text 'Open Data Drug & Drug Target Database'. Below the header is a navigation menu with 'Home', 'Browse', 'Search', 'Downloads', 'News & Updates', 'About', 'Help', and 'Contact Us'. A search bar is present with the text 'Search: Search DrugBank' and buttons for 'Search' and 'Help / Advanced'. The main content area contains a paragraph describing the database's unique bioinformatics and cheminformatics resource. Below this is a section about search capabilities and a 'What's New?' section.

<http://www.drugbank.ca>

The Human Metabolome Database (HMDB)

The screenshot displays the HMDB website interface. At the top, there is a navigation bar with 'Home', 'Browse', 'Search', 'About', 'Downloads', and 'Contact Us'. Below this is the 'Human Metabolome Database' header with a search bar and the HMDB logo. A paragraph of text describes the database's scope and features. Below the text is a 'What's New?' section dated November 5, 2009. The main content area is titled 'Metabolomics Toolbox' and shows a 'Browsing biofluids' section with a table of metabolites.

HMDB ID	Name	Concentration Range (µmol/L)	Patient Status	Age	Sex	Reference
HMDB00011 (Metabocard)	(R)-3-Hydroxybutyric acid	286 (207-365) µM	normal Normal	Adult >18 yrs old	Both	Subramanian A, Gupta A, Sena S, Gupta A, Kumar M, Nagar A, Kumar A, Mandal SK, Roy R, Prasad MR. MS/MS analysis and a new software as predictors for the identification of meringitis in children. <i>Metab. Horm. 2008 Jun;18(4):273-76. PubMed</i>
HMDB00011 (Metabocard)	(R)-3-Hydroxybutyric acid	430 (350-501) µM	abnormal Bacterial meningitis	Adult >18 yrs old	Both	Subramanian A, Gupta A, Sena S, Gupta A, Kumar M, Nagar A, Kumar A, Mandal SK, Roy R, Prasad MR. MS/MS analysis and a new software as predictors for the identification of meringitis in children. <i>Metab. Horm. 2008 Jun;18(4):273-76. PubMed</i>

<http://www.hmdb.ca>

- A web-accessible resource containing detailed information on 40214 “quantified”, “detected” and “expected” metabolites
- Normal/abnormal concentrations
- 600+ disease links
- 1000’s of reference spectra
- 1000’s of reactions & pathways
- Supports sequence, spectral, structure and text searches as well as compound browsing
- Full data downloads

The Food Constituent Database (FooDB)

The screenshot displays the FooDB website interface. The top navigation bar includes 'Home', 'Browse', 'DrugBank', and 'HMDB'. The main content area shows a search for 'Catechin' with a table of results. The table lists various food categories and their corresponding catechin concentrations. Below the table, there is a detailed view for 'Catechin' (FooDB ID 1), including its chemical structure, creation and update dates, and a description. The description states: 'Catechin is a polyphenolic antioxidant plant metabolite. The term catechin is also commonly used to refer to the related family of flavonoids and the subgroup flavan-3-ols (or simply flavanols). Catechins are differentiated from the ketone-containing flavonoids such as quercetin and rutin, which are called flavonols (spelled flavonols with an o). The term bioflavonoid was first used to describe the flavonols, but as an imprecise term has been loosely applied to the larger family of flavonoids, including also the polymeric hydroxyl-only containing flavan-3-ols'.

Content in Foods	Concentration
Alcoholic beverages	
Beers	
Beer [Alcohol free]	0.10 mg/100 ml
Beer [Ale]	0.33 mg/100 ml
Beer [Dark]	0.02 mg/100 ml
Beer [Regular]	0.11 mg/100 ml
Liquors - Nut liquors	
Walnut, liquor	1.55 mg/100 ml
Wines - Fortified Wines	
Sherry	2.37 mg/100 ml
Wines - Grape wines	
Wine [Red]	6.81 mg/100 ml
Wine [Rose]	0.91 mg/100 ml
Wine [White]	1.08 mg/100 ml
Wines - Sparkling wines	
Champagne	0.20 mg/100 ml
Cereals and cereal products	
Cereals	
Barley, whole grain flour	1.23 mg/100 g FW
Cocoa	
Cocoa - Chocolate	
Chocolate, dark	20.50 mg/100 g FW
Chocolate, milk	4.64 mg/100 g FW

Property	Reference
Improves life expectancy	Beneficial effects of natural antioxidants EGCG and alpha-lipoic acid on life span and age-dependent behavioral declines in <i>Caenorhabditis elegans</i> . Brown MK, Evans JL, Luo Y. <i>Pharmacol Biochem Behav.</i> 2006 Nov;85(3):620-8. Epub 2006 Dec 5. [PubMed: 17158333]
Shown to possess antibiotic properties	Gradisar H, Pristovsek P, Plaper A, Jerala R (January 2007). "Green tea catechins inhibit bacterial DNA gyrase by interaction with its ATP binding site". <i>J. Med. Chem.</i> 50 (2): 264-71. doi:10.1021/jm060817o. [PubMed: 17228868]
Epicatechin can reduce the risk of four of the major health problems: stroke, heart failure, cancer and diabetes	Science Daily March 12, 2007.

- 28,543 compounds, 24,579 structures with 21,843 descriptions
- 131,867 synonyms
- 3000 flavour-compound associations
- Content data on 635 “pure” foods
- >60,000 hyperlinks to 11 different external DBs
- Supports sequence, structure & text searches
- >100 data fields/cmpd
- Not quite “Live”

<http://www.foodb.ca>

The E. coli Metabolome Database (ECMDB)

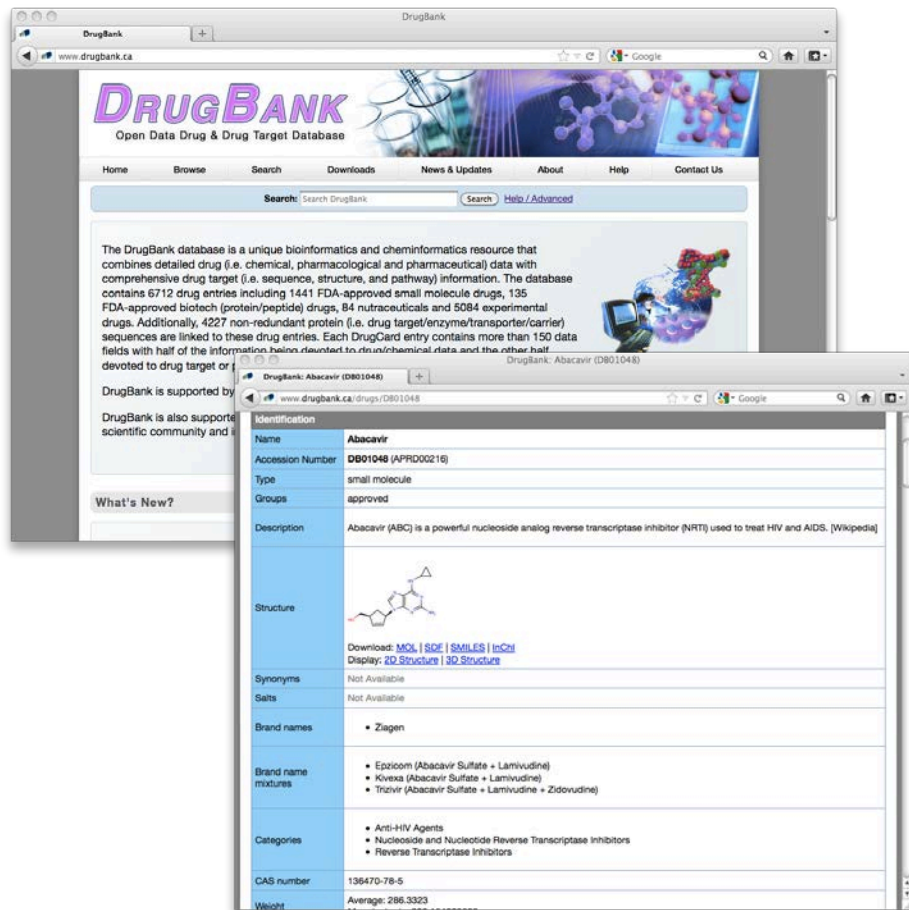
The screenshot shows the ECMDB website interface. The top part is the homepage with a navigation menu (Home, Browse, Search, About, Help, Downloads, Contact Us) and a search bar. Below the navigation is a paragraph describing the database. The bottom part of the screenshot shows a search results table with columns for ECMDB ID, Name, CAS Number, IUPAC Name, Formula, Weight, and Structure. The table lists three entries: 2-Ketobutyric acid, Deoxyuridine, and Deoxycytidine.

ECMDB ID	Name	CAS Number	IUPAC Name	Formula	Weight	Structure
ECMDB00005 MetaboCard	2-Ketobutyric acid	600-18-0	2-oxobutanoic acid	C ₄ H ₆ O ₃	102.0866	
ECMDB00012 MetaboCard	Deoxyuridine	951-78-0	4-hydroxy-1-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,2-dihydropyrimidin-2-one	C ₉ H ₁₂ N ₂ O ₅	228.202	
ECMDB00014 MetaboCard	Deoxycytidine	661-77-9	1-[(2R,4S,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-4-imino-1,4-dihydropyrimidin-2-ol	C ₉ H ₁₂ N ₂ O ₅	227.2172	


- 2717 E. coli metabolites
- 1573 genes (1205 enzymes, 299 transporters)
- 3145 chemical reactions
- 4300 references
- 125 pathways
- Supports sequence, structure & text searches as well as compound browsing
- 80 data fields per compound
- 4965 NMR and MS spectra
- Corrects many errors and erroneous entries in EcoCyc

<http://www.ecmdb.ca>

The Drug Database (DrugBank)



The DrugBank website interface is shown, featuring a search bar and a navigation menu. The main content area displays a description of the database and a 'What's New?' section. An inset window shows the detailed entry for Abacavir (DB01048), including its chemical structure and various identifiers.

Identification	
Name	Abacavir
Accession Number	DB01048 (APRD00216)
Type	small molecule
Groups	approved
Description	Abacavir (ABC) is a powerful nucleoside analog reverse transcriptase inhibitor (NRTI) used to treat HIV and AIDS. [Wikipedia]
Structure	 Download: MOL , SDF SMILES InChI Display: 2D Structure 3D Structure
Synonyms	Not Available
Salts	Not Available
Brand names	<ul style="list-style-type: none">Ziagen
Brand name mixtures	<ul style="list-style-type: none">Epizoom (Abacavir Sulfate + Lamivudine)Kivexa (Abacavir Sulfate + Lamivudine)Trizivir (Abacavir Sulfate + Lamivudine + Zidovudine)
Categories	<ul style="list-style-type: none">Anti-HIV AgentsNucleoside and Nucleotide Reverse Transcriptase InhibitorsReverse Transcriptase Inhibitors
CAS number	136470-78-5
Weight	Average: 286.3323

- 1447 small molecule drugs
- 85 nutraceuticals
- >500 drug metabolites
- >5200 experimental drugs
- 148 data fields/drug
- >1000 food/drug interacts
- 1637 drug targets
- >200 drug pathways
- Supports sequence, spectral, structure and text searches as well as compound browsing
- Full data downloads

<http://www.drugbank.ca>

A Word About DrugBank..

- First database to link drugs to drug targets**
- Intended to facilitate systems and predictive pharmacology and to accelerate drug R&D pipeline**
- Receives ~7 million web hits/year, linked to all major bioinformatic databases and used by all major pharmaceutical companies**
- Has been used to discover, design and repurpose a number of drugs**
- Our model for T3DB...**

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Microbial metabolites

28500 (FooDB)

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1450 (DrugBank)

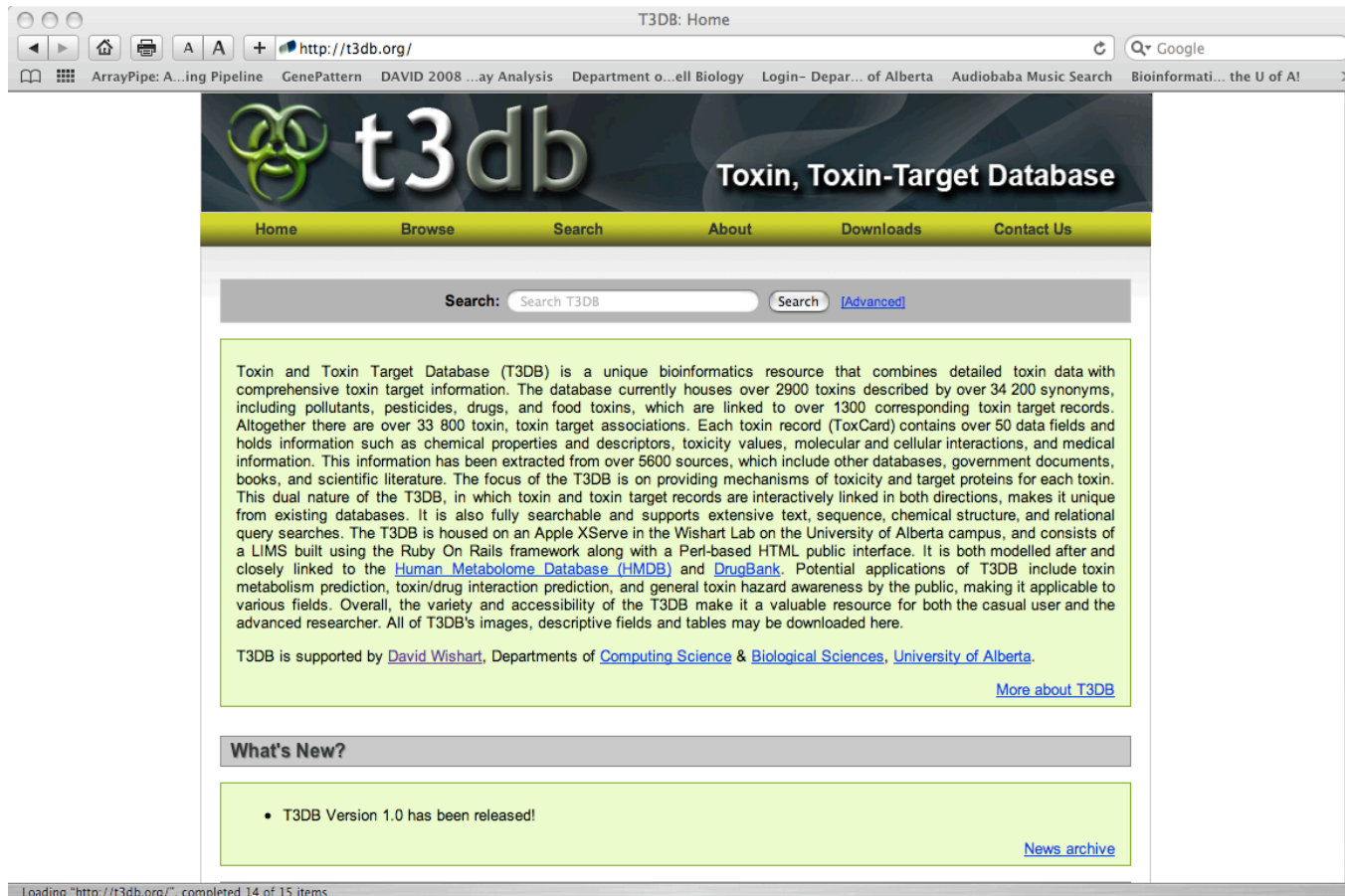
Drugs

19700 (HMDB)

Endogenous metabolites



The Toxin, Toxin-Target Database (T3DB)



The screenshot shows the T3DB website homepage in a web browser. The browser's address bar displays "http://t3db.org/". The website header features the T3DB logo, which consists of a green biohazard symbol and the text "t3db". To the right of the logo, the text "Toxin, Toxin-Target Database" is displayed. Below the header is a navigation menu with links for "Home", "Browse", "Search", "About", "Downloads", and "Contact Us". A search bar is located below the navigation menu, with the text "Search: Search T3DB" and a "Search" button. A link for "Advanced" search is also present. The main content area contains a paragraph of text describing the database, followed by a "What's New?" section with a bullet point stating "T3DB Version 1.0 has been released!".

T3DB: Home

http://t3db.org/

ArrayPipe: A...ing Pipeline GenePattern DAVID 2008 ...ay Analysis Department o...ell Biology Login- Depar... of Alberta Audiobaba Music Search Bioinformati... the U of A

 t3db Toxin, Toxin-Target Database

Home Browse Search About Downloads Contact Us

Search: Search T3DB Search [Advanced](#)

Toxin and Toxin Target Database (T3DB) is a unique bioinformatics resource that combines detailed toxin data with comprehensive toxin target information. The database currently houses over 2900 toxins described by over 34 200 synonyms, including pollutants, pesticides, drugs, and food toxins, which are linked to over 1300 corresponding toxin target records. Altogether there are over 33 800 toxin, toxin target associations. Each toxin record (ToxCard) contains over 50 data fields and holds information such as chemical properties and descriptors, toxicity values, molecular and cellular interactions, and medical information. This information has been extracted from over 5600 sources, which include other databases, government documents, books, and scientific literature. The focus of the T3DB is on providing mechanisms of toxicity and target proteins for each toxin. This dual nature of the T3DB, in which toxin and toxin target records are interactively linked in both directions, makes it unique from existing databases. It is also fully searchable and supports extensive text, sequence, chemical structure, and relational query searches. The T3DB is housed on an Apple XServe in the Wishart Lab on the University of Alberta campus, and consists of a LIMS built using the Ruby On Rails framework along with a Perl-based HTML public interface. It is both modelled after and closely linked to the [Human Metabolome Database \(HMDB\)](#) and [DrugBank](#). Potential applications of T3DB include toxin metabolism prediction, toxin/drug interaction prediction, and general toxin hazard awareness by the public, making it applicable to various fields. Overall, the variety and accessibility of the T3DB make it a valuable resource for both the casual user and the advanced researcher. All of T3DB's images, descriptive fields and tables may be downloaded here.

T3DB is supported by [David Wishart](#), Departments of [Computing Science](#) & [Biological Sciences](#), [University of Alberta](#).

[More about T3DB](#)

What's New?

- T3DB Version 1.0 has been released!

[News archive](#)

Loading "http://t3db.org/", completed 14 of 15 items

Lim E, Pon A, Djoumbou Y, Knox C, Shrivastava S, Guo AC, Neveu V, Wishart DS. T3DB: a comprehensively annotated database of common toxins and their targets. *Nucleic Acids Res.* 2010 Jan 38(Database issue):D781-6. <http://www.t3db.org>

The Toxin, Toxin-Target Database (T3DB)

The screenshot displays the T3DB website interface. The top navigation bar includes links for Home, Browse, Search, About, Downloads, and Contact Us. A search bar is present with the text "Search T3DB" and a "Search" button. Below the search bar, the page indicates "Browsing toxins" and "Showing 1-10 out of 2910". A table lists toxins, with the first entry being Digoxin (T3D02670). The detailed profile for Digoxin is shown below, including fields for Predicted LogP, Route of Exposure, Mechanism of Action, Metabolism, Toxicity Values, Lethal Dose, Carcinogenicity (ARC Classification), Uses/Sources, Minimum Risk Level, Health Effects, Symptoms, and Treatment.

T3DB ID	Name	Formula	Structure	Compound Type	Mechanism of Action
T3D0001 ToxinCard	Digoxin	C ₄₁ H ₆₄ O ₁₁		Cardiac Glycoside	Na ⁺ /K ⁺ ATPase Inhibitor
T3D0002 ToxinCard	Digoxigenin	C ₄₁ H ₆₄ O ₁₀		Cardiac Glycoside	Na ⁺ /K ⁺ ATPase Inhibitor

Predicted LogP: 2.3667

Route of Exposure: Ingestion or dermal contact. (W468)

Mechanism of Action: Digoxin binds to a site on the extracellular aspect of the alpha-subunit of the Na⁺/K⁺ ATPase pump in the membranes of heart cells (myocytes) and decreases its function. This causes an increase in the level of sodium ions in the myocytes. This effect causes an increase in the length the cardiac action potential, which when combined with the effects of digoxin on the parasympathetic nervous system, lead to a decrease in heart rate. Increased amounts of calcium are then stored in the sarcoplasmic reticulum and released by each action potential, which is unchanged by digoxin. This leads to increased contractility of the heart. Digoxin also increases vagal activity via its action on the central nervous system, thus decreasing the conduction of electrical impulses through the AV node. (S805)

Metabolism: Hepatic (but not dependent upon the cytochrome P-450 system). The end metabolites, which include 3 b-digoxigenin, 3-keto-digoxigenin, and their glucuronide and sulfate conjugates, are polar in nature and are postulated to be formed via hydrolysis, oxidation, and conjugation.

Toxicity Values: Not Available

Lethal Dose: Not Available

Carcinogenicity (ARC Classification): Not Available

Uses/Sources: Digoxin is a plant toxin found in the foxglove plant (*Digitalis lanata*). It is used as a drug to treat various heart conditions, namely atrial fibrillation, atrial flutter and sometimes heart failure. (S805)

Minimum Risk Level: Not Available

Health Effects: Digoxin mainly affects the heart. (S805)

Symptoms: Adverse effects of digoxin include loss of appetite, nausea, vomiting, diarrhea, blurred vision, visual disturbances (yellow-green halos), confusion, drowsiness, dizziness, nightmares, agitation, and/or depression, as well as a higher acute sense of sensual activities. (S805)

Treatment: Treatment of dioxin overdose includes supportive measure and administration of the antidote, antidigoxin (DIGIBIND). Toxicity can also be treated with higher than normal doses of potassium. (S805)

• S805 - Wikipedia. Digoxin. Last Updated 8 July 2009.
• UKOL - Karlamangla J, Weinhausen F, Tronez M, Genovik G, Varanasi and Rinovik. Interactions in the rat

- >2900 common toxins (drugs, pesticides, herbicides, cosmetic compounds, cleaners, solvents, PCBs, furans, etc.)
- 1550 toxin targets – **now including ToxCast targets**
- 406 toxin “classes”
- Describes MOA, toxic effects, treatment, lethal or harmful dose
- 80 data fields per compound including data on protein targets (if known)

<http://www.t3db.org>

A Word About T3DB..

- **First database to link common toxins/poisons to specific human targets**
- **Intended to help with systems toxicology**
- **Intended to facilitate *in silico* toxicity or mechanism of action testing**
- **Intended to enable predictive toxicology (via sequence/structure/QSAR mapping)**
- **Largely unknown in the tox community**
- **Hoping to find out ways of making it more useful/appealing to the community**

Inside T3DB – Browsing Options

T3DB: Browse

www.t3db.org/toxins?page=1;per_page=10;sort_by=title;sort_order=desc

Home Browse Search About Downloads Contact Us

Search: Search T3DB Search [Advanced]

Browsing toxins

Per Page: 10 | 25 | 50 | 100

Showing 1-10 out of 3023

previous 1 2 3 4 5 6 7 8 9 10 11 ... 302 303 next

T3DB ID	Name	Formula	Structure	Compound Type	Mechanism of Action
	CAS Number	Weight			
T3D0001 ToxinCard	Arsenic 7440-38-2	[As] ³⁺ 74.921600	As	Arsenic Compound Inorganic Compound Metalloid	Arsenic and its metabolites disrupt ATP production through several mechanisms. At the level of the citric acid cycle, arsenic inhibits pyruvate dehydrogenase and by competing ...
T3D0002 ToxinCard	Lead 7439-92-1	[Pb] ²⁺ 207.976654	Pb	Inorganic Compound Lead Compound Metal	Lead mimics other biologically important metals, such as zinc, calcium, and iron, competing as cofactors for many of their respective enzymatic reactions. For example, lead ha...
T3D0003 ToxinCard	Mercury 7439-97-6	[Hg] ²⁺ 201.970642	Hg	Cosmetic Toxin Inorganic Compound Mercury Compound Metal	High-affinity binding of the divalent mercuric ion to thiol or sulfhydryl groups of proteins is believed to be the major mechanism for the activity of mercury. Through alterat...
T3D0004 ToxinCard	Vinyl chloride 75-01-4	C ₂ H ₃ Cl 61.992330	<chem>ClC=CH2</chem>	Industrial Precursor/Intermediate Organic Compound Organochloride	Vinyl chloride poisoning exhibits many of the characteristics of autoimmune diseases. This is believed to be the result of a reactive vinyl chloride intermediate metabolite...

Browse by Compound

T3DB: Type Browse

www.t3db.org/type_browse

T3D2862 Tizanidine

Parasympathomimetic (5 toxins)

T3DB ID Common Name

T3D2958 Bethanechol

T3D2910 Donepezil

T3D2857 Galantamine

T3D2820 Pyridostigmine

T3D2772 Tacrine

Perchlorate (5 toxins)

T3DB ID Common Name

T3D1914 Ammonium perchlorate

T3D1916 Lithium perchlorate

T3D1912 Magnesium perchlorate

T3D1913 Potassium perchlorate

T3D1915 Sodium perchlorate

Peripheral Adrenergic Inhibitor (1 toxin)

T3DB ID Common Name

T3D2713 Reserpine

Pesticide (295 toxins)

T3DB ID Common Name

T3D1078 (11E)-11-(Nitromethylidene)-[1]benzofuro[3,2-b]chromene

T3D1062 (2E)-1-Methyl-2-(nitromethylidene)pyrrolidine

T3D1055 (2E)-2-(Nitromethylidene)-1,3-thiazinane

T3D1059 (2E)-2-(Nitromethylidene)-1-prop-2-enylpyrrolidine

T3D1051 (2E)-3-Benzyl-2-(nitromethylidene)-1,3-thiazolidine

T3D1062 (2E)-3-Methyl-2-(nitromethylidene)imidazole-1-carboximidamide...

T3D1060 (2Z)-1-Benzyl-2-(nitromethylidene)pyrrolidine

T3D1058 (2Z)-1-Ethyl-2-(nitromethylidene)pyrrolidine

T3D1047 (2Z)-1-Methyl-2-(nitromethylidene)pyrrolidine

T3D1083 (2Z)-2-(Nitromethylidene)-3-[4-(trifluoromethoxy)phenyl]-1,3...

T3D1057 (2Z)-2-(Nitromethylidene)-1,3-thiazolidine

T3D1068 (2Z)-2-(Nitromethylidene)-3-phenyl-1,3-thiazolidin-4-one

Browse by Toxin Type

Inside T3DB – Search Options

The screenshot shows the T3DB ChemQuery search interface. The browser address bar displays "www.t3db.org/search/chemquery". The page header includes the T3DB logo and navigation links: Home, Browse, Search, About, Downloads, and Contact Us. A search bar is present with the text "Search: Search T3DB" and a "Search" button. Below the search bar, the "ChemQuery" section is active, with sub-options for "Structure", "SMILES", and "Molecular Weight". The main content area features a search type selector (radio buttons for "Tanimoto Similarity", "Substructure", and "Exact"), a similarity threshold of 0.7, and a molecular weight filter. A "Maximum Results Returned" dropdown is set to 100. A "Search" button is located at the bottom left. On the right, a chemical structure editor is open, showing a chemical structure of a bispyridinium salt with two methyl groups and two chloride counterions. The editor includes a menu bar (File, Edit, View, Insert, Atom, Bond, Structure, Tools, Help) and a toolbar with various drawing tools.

Search by Structure

The screenshot shows the T3DB Sequence Query search interface. The browser address bar displays "www.t3db.org/search/seqquery". The page header includes the T3DB logo and navigation links: Home, Browse, Search, About, Downloads, and Contact Us. A search bar is present with the text "Search: Search T3DB" and a "Search" button. Below the search bar, the "Sequence Search" section is active. The main content area features a text input field with the instruction "Paste query sequence(s) in FASTA Format below". The input field contains a multi-line FASTA format sequence starting with ">query1" followed by amino acid sequences. Below the input field, the "BLAST Parameters" section is visible, including dropdown menus for "Program/Sequence Type" (set to "blastp (protein seq)"), "Scoring Matrix" (set to "BLOSUM62"), and "Alignment View" (set to "Pairwise"). There are also checkboxes for "Perform gapped alignment" (checked), "Lower case filtering of FASTA sequence" (unchecked), and "Filter query sequence (DUST & SEG)" (checked). The "Expectation value" is set to 0.00001.

Search by Sequence

Inside T3DB – Toxin Cards or ToxCards

T3DB: Showing Lead tetroxide (T3D0332)

Showing toxin card for Lead tetroxide (T3D0332)

Legend: **toxin field** **target field** [Show Similar Structures](#)

Version	1.0
Creation Date	2009-03-06 18:58:33
Update Date	2010-03-18 21:52:42
Accession Number	T3D0332
Name	Lead tetroxide
Compound Type	<ul style="list-style-type: none">Inorganic CompoundLead Compound
Description	Lead tetroxide is an oxide of lead the occurs naturally as the mineral minium. It is most often used in the production of batteries, pigments and lead glass. Lead is a heavy metal and stable element with the symbol Pb and the atomic number 82, existing in metallic, organic, and inorganic forms. It is mainly found in nature as the mineral galena (PbS), cerussite (PbCO3) or anglesite (PbSO4), usually in ore with zinc, silver, or copper. (R056, R702)
	<ol style="list-style-type: none">BleimonoxidBleioxydC.I. Pigment Yellow 46C.I. Pigment red 105CI Pigment Red 105CI Pigment Yellow 46Gold satinobreHeuconin 5Lead monooxideLead monoxideLead orthoplumbateLead oxideLead oxide (Pb3O4)Lead oxide (pbo)Lead oxide (van)Lead oxide red

T3DB: Showing Lead tetroxide (T3D0332)

Metabolism	Lead is absorbed following inhalation, oral, and dermal exposure. It is then distributed mainly to the bones and red blood cells. In the blood lead may be found bound to serum albumin or the metal-binding protein metallothionein. Organic lead is metabolized by cytochrome P-450 enzymes, whereas inorganic lead forms complexes with delta-aminolevulinic acid dehydratase. Lead is excreted mainly in the urine and faeces. (R266)
Toxicity Values	LD50: 630 mg/kg (Intraperitoneal, Rat) (R263)
Lethal Dose	10 to 30 grams for and adult human (lead salts), (R273)
Carcinogenicity (IARC Classification)	2B, possibly carcinogenic to humans. (R264)
Uses/Sources	Lead tetroxide is used the production of batteries, pigments, and lead glass. (R702)
Minimum Risk Level	Chronic Inhalation: 0.05 mg/m3 (R260)
Health Effects	Lead is a neurotoxin and has been known to cause brain damage and reduced cognitive capacity, especially in children. Lead exposure can result in nephropathy, as well as blood disorders such as high blood pressure and anemia. Lead also exhibits reproductive toxicity and can results in miscarriages and reduced sperm production. (R056)
Symptoms	Symptoms of chronic lead poisoning include reduced cognitive abilities, nausea, abdominal pain, irritability, insomnia, metal taste in the mouth, excess lethargy or hyperactivity, chest pain, headache and, in extreme cases, seizures, comas, and death. There are also associated gastrointestinal problems, such as constipation, diarrhea, vomiting, poor appetite, weight loss, which are common in acute poisoning. (R007, R056)
Treatment	Lead poisoning is usually treated with chelation therapy using DMSA, EDTA, or dimercaprol. (R056)
	<ul style="list-style-type: none">R264 - International Agency for Research on Cancer (2009). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.R008 - Ellenhorn MJ and Barceloux DG (1998). Diagnosis and treatment of human poisoning. Medical Toxicology. New York, New York: Elsevier Science Publishing Company, Inc.R061 - Gill KD, Gupta V, Sandhir R. Ca2+/calmodulin-mediated neurotransmitter release and neurobehavioural deficits following lead exposure. Cell Biochem Funct. 2003 Dec;21(4):345-53. [PubMed]R702 - Wikipedia. Lead tetroxide. Last Updated 27 April 2009.R266 - ATSDR - Agency for Toxic Substances and Disease Registry (2007). Toxicological profile for lead. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).

Lead Tetraoxide

Inside T3DB – Protein (Target) Cards

T3DB: Showing Tacrine (T3D2772)

www.t3db.org/toxins/T3D2772

Target 1 [top]	
Target 1 ID	312
Target 1 Name	Acetylcholinesterase
Target 1 Mechanism of Action	Tacrine acts by elevating acetylcholine concentrations in the cerebral cortex by slowing the degradation of acetylcholine released by still intact cholinergic neurons. It does so by reversibly binding acetylcholinesterase.
Target 1 Description	Terminates signal transduction at the neuromuscular junction by rapid hydrolysis of the acetylcholine released into the synaptic cleft. Role in neuronal apoptosis
Target 1 Synonyms	1. AChE
Target 1 Gene Name	ACHE
Target 1 Protein Sequence	>Acetylcholinesterase MRFPQCLLHTPPLASPLLLLLLLWLLGGCVGAGSREDAELLVTVRGGRLGIRLKTGCGFV SAFLGIPFAEPPKPRRFLPPPEPKQWGVDAITFGSVCYQVDTLYPGEFETMHWNP RELSEDCILYLNWVTPYRPTSPTPVLVNIYGGFYSGASSLDVYDGRFLVQERTVLVSM NRYVGAFCPLALPGSREAPGMVGLDQRLALQWVQSNVAAPGGDPTVTLFGEAGASV GMHLLSPPSRGLFHRVAVLQSGAPNGPWATVGMGEARRATQLAHLVGCPPGTGGNDTEL VACLRTFPAQVLVNHVHVLQESVFRFSFVFPVVDGDFLSDTPEALINAGDFHGLQVLVG VVKDEGSFLVYGAQFSGKNSLSISRAEFLAGVRRVQVQVSDLAASNVLHYDNLHPE DPAKLEALSDVGDHNVCPVAQLAGRLAQGARVYAVYFIRASTLSPLMWVPHGY EIEFIFGIPLDPSRNYTAEKIFAQRLMRWYANFARTGDPNEPRDPKAPQWPPYTAGAQQ YVSLDLRPLVRRRLAQACAFWNRFLPKLLSATDTLDEAERQWKAEFHRWSSYMHWN QPDHYSKQDCRSDL
Target 1 Number of Residues	614
Target 1 Molecular Weight	67795.5
Target 1 Theoretical pI	6.24

T3DB: Showing Tacrine (T3D2772)

www.t3db.org/toxins/T3D2772

Target 1 GO Classification	<p>Function</p> <ul style="list-style-type: none"> catalytic activity hydrolase activity hydrolase activity, acting on ester bonds carboxylic ester hydrolase activity cholinesterase activity <p>Process</p> <ul style="list-style-type: none"> Not Available <p>Component</p> <ul style="list-style-type: none"> Not Available
Target 1 General Function	Lipid transport and metabolism
Target 1 Pathways	Not Available
Target 1 Reactions	Not Available
Target 1 Signals	<ul style="list-style-type: none"> 1-31
Target 1 Transmembrane Regions	<ul style="list-style-type: none"> None
Target 1 Essentiality	Non Essential
Target 1 Domain Function	PF08674:ACHE_tetra PF00135:COesterase
Target 1 GenBank ID Protein	Not Available
Target 1 UniProtKB ID	P22303
Target 1 Cellular Location	Isoform H:Cell membrane

Acetylcholinesterase

Inside T3DB – Complex Queries & Data Extraction

The screenshot shows a web browser window titled "T3DB: Data Extractor" with the URL "www.t3db.org/search/extractor". The page features the T3DB logo and the text "Toxin, Toxin-Target Database". A navigation menu includes "Home", "Browse", "Search", "About", "Downloads", and "Contact Us". A search bar contains the text "Search: Search T3DB" and a "Search" button, with a link to "[Advanced]".

Data Extractor

The Data Extractor is a high level data search engine which allows users to construct complex or constrained queries and to select or display search results from the T3DB databases. To use the Data Extractor, select the fields you want to search on the left and enter your query. You can select to view the results in HTML, a printable list, or CSV (which you can open in Microsoft Excel).

- Use an asterisk (*) to match any non-blank value for a field
- For text search, the query text can be either whole or partial words
- Leave a field blank to include it in the output, but omit it from the search
- We do not recommend opening complex CSV files with Microsoft Excel, as it does not handle newlines correctly. If you experience any issues with the CSV format in Microsoft Excel, please try loading the data into OpenOffice or Numbers before reporting any issues.

Legend: toxin field target field

Toxin Fields:	Name	Value	Description
<input type="checkbox"/> Appearance	Name	*	Full or partial text (i.e. arsenic or ar)
<input type="checkbox"/> Boiling Point (°C)	Compound Type	*	Full or partial text (i.e. metallic)
<input type="checkbox"/> CAS Number	Melting Point (°C)	min: 130 max: 150	Numeric range (i.e. 24.4)
<input checked="" type="checkbox"/> Name	Solubility	min: 12 max: 130	Numeric range (i.e. 24.4)
<input checked="" type="checkbox"/> Compound Type	T3DB ID	*	Full or partial text (i.e. T3D0001 or T3D0003)
<input type="checkbox"/> Description			
<input type="checkbox"/> Mechanism of Action			
<input checked="" type="checkbox"/> Melting Point (°C)			
<input type="checkbox"/> PubChem Compound ID			
<input checked="" type="checkbox"/> Solubility			
<input type="checkbox"/> Synonyms			
<input checked="" type="checkbox"/> T3DB ID			

ToxCard - Paraquat

T3DB: Showing Paraquat (T3D0808)

www.t3db.org/toxins/T3D0808

t3db Toxin, Toxin-Target Database

Home Browse Search About Downloads Contact Us

Search: Search T3DB Search [Advanced](#)

Showing toxin card for Paraquat (T3D0808)

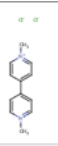
Legend: **toxin field** **target field** [Show Similar Structures](#)

Version	1.0
Creation Date	2009-06-03 21:56:02
Update Date	2012-09-23 16:41:26
Accession Number	T3D0808
Name	Paraquat
Compound Type	<ul style="list-style-type: none">• Aromatic Hydrocarbon• Herbicide• Organic Compound
Description	Paraquat is the trade name for N,N'-dimethyl-4,4'-bipyridinium dichloride, one of the most widely used herbicides in the world. Paraquat, a viologen, is quick-acting and non-selective, killing green plant tissue on contact. It is also toxic to human beings when swallowed (R714).
	<ol style="list-style-type: none">1. 1,1'-Dimethyl-4,4'-bipyridinium dichloride2. 1,1'-Dimethyl-4,4'-dipyridylum chloride3. 1,1'-Dimethyl-4,4'-bipyridinium dichloride4. 1,1'-Dimethyl-4,4'-bipyridinium dichloride hydrate5. 1,1'-Dimethyl-4,4'-bipyridinium dichloride6. 1,1'-Dimethyl-4,4'-dipyridinium-dichlorid [German]7. 1,1'-Dimethyl-4,4'-dipyridylum dichloride8. 1,1'-dimethyl-[4,4'-bipyridin]-1,1'-dium dichloride9. 1,1-Dimethyl-4,4-dipyridylum dichloride10. 4,4'-Bipyridinium, 1,1'-dimethyl-, dichloride11. 4,4'-Dimethyldipyridyl dichloride12. Bipyridinium, 4,4'-dimethyl-4,4'-dichloride

ToxCard - Paraquat

T3DB: Showing Paraquat (T3D0808)

www.t3db.org/toxins/T3D0808

	39. Parakwat [polish] 40. Paraquat chloride 41. Paraquat dichloride 42. Paraquat-dichloride 43. Pathclear 44. Pillarquat 45. Pillarxone 46. Toxer total 47. Viologen, methyl-
Chemical IUPAC Name	1-methyl-4-(1-methylpyridin-1-ium-4-yl)pyridin-1-ium dichloride
Chemical Formula	C ₁₂ H ₁₄ Cl ₂ N ₂
Chemical Structure	
CAS Registry Number	1910-42-5
InChI Identifier	InChI=1S/C12H14N2.2ClH/c1-13-7-3-11(4-8-13)12-5-9-14(2)10-6-12;;/h3-10H,1-2H3;2*1H/q+2;;/p-2
InChI Key	InChIKey=FIKAKWIAUPDISJ-UHFFFAOYSA-L
PubChem Compound ID	15938
KEGG ID	C00225
UniProt ID	
OMIM ID	Not Available
ChEBI ID	28786
BioCyc ID	Not Available
SuperToxic ID	Not Available
CTD ID	Not Available
Stitch ID	Paraquat
DrugBank ID	Not Available

ToxCard - Paraquat

T3DB: Showing Paraquat (T3D0808)

www.t3db.org/toxins/T3D0808

Predicted LogP	-6.7016
Route of Exposure	Inhalation (R502) ; oral (R502) ; eye contact (R502) ; dermal (R502)
Mechanism of Action	The mechanisms of the toxic effects of paraquat are largely the result of a metabolically catalyzed single electron oxidation reduction reaction, resulting in depletion of cellular NADPH and the generation of potentially toxic forms of oxygen such as the superoxide radical (S400). Recent studies have demonstrated paraquat cytotoxicity occurs in the mitochondria and particularly in mitochondrial-rich tissues. The mitochondrial NADH-dependent PQ reductase containing a voltage-dependent anion channel 1 (VDAC1) appears to be largely responsible for paraquat cytotoxicity. When mitochondria are incubated with NADH and paraquat, the superoxide anion is produced, and the mitochondria rupture. Ruptured mitochondria lead to rapid cell death (W969).
Metabolism	Paraquat is poorly absorbed after oral exposure. It is not metabolized but is reduced to an unstable free radical which is then re-oxidized to reform the cation and produce a superoxide anion. It is excreted mostly in the urine, and in small fraction also in the feces (S399, S401).
Toxicity Values	LD50: 150 mg/kg (Oral, Rat) (S401) LD50: >480 mg/kg (Dermal, Rabbit) (S401)
Lethal Dose	35 mg/kg
Carcinogenicity (IARC Classification)	Not Available
Uses/Sources	Paraquat is used as a quaternary ammonium herbicide; one of the most widely used herbicides in the world. It is also often used in science to catalyze the formation of reactive oxygen species (ROS). (R714).
Minimum Risk Level	Not Available
Health Effects	It can cause temporary damage to nails and if swallowed, may cause nose bleeding. Long term exposures to paraquat would most likely cause lung and eye damage. Some suspect a possible link to a greater incidence of Parkinson's disease. Pancreatitis may develop in some cases of acute. Paraquat is caustic to the oral, esophageal, and gastric mucosa (R383, R1010, R714).
Symptoms	Eye or skin irritation; hypotension may develop after large ingestion; epistaxis and sore throat may develop after inhalation. Nausea, vomiting, diarrhea, and abdominal pain are common (R383).
Treatment	In case of oral exposure, administer charcoal as a slurry. Consider after ingestion of a potentially life-threatening amount of poison if it can be performed soon after ingestion. The treatment is symptomatic and supportive. In case of eye exposure, irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. In case of dermal exposure, remove contaminated clothing and jewellery. Wash the skin, including hair and nails, vigorously; do repeated soap washings. Discard contaminated clothing. (R383)
	<ul style="list-style-type: none"> R383 - Rumack BH (2009). POISINDEX(R) Information System. Englewood, CO: Micromedex, Inc. CCIS Volume 141, edition expires Aug, 2009. R1010 - Worthing, CR and SB Walker (1987). The Pesticide Manual - A World Compendium. 8th ed. Thornton Heath, UK: The British Crop Protection Council.

Paraquat via ACToR

Generic Chemical | ACToR | US EPA

actor.epa.gov/actor/GenericChemical?casrn=4685-14-7

EPA United States Environmental Protection Agency

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ACToR National Center for Computational Toxicology » ACToR » Generic Chemical

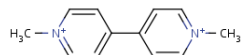
ACToR | ToxRefDB | ToxCastDB | ExpoCastDB | DSSTox

Home | Basic Info | Data Collections | Structure Search | Assays By Toxicity | Assays By Category | External Links | Download | Help

Chemical: Paraquat

PDF Version

Email link to this page: <http://actor.epa.gov/actor/GenericChemical?casrn=4685-14-7>



Synonyms

- "1,1'-Dimethyl-4,4'-bipyridinium ion"
- "1,1'-Dimethyl-4,4'-bipyridinium"

Home | ACToR | US EPA

actor.epa.gov/actor/faces/ACToRHome.jsp

Chemical Name Parameters Match by

Search on Chemical Names exact

Search on CAS Numbers any

Enter Chemical Name:

paraquat

Search

Search Results

Details	Image	CASRN	Preferred Name	Chronic		Developmental	Reproductive	Food		
				Hazard	Toxicity				Carcinogenicity	Genotoxicity
details		1910-42-5	Paraquat dichloride	Ha	Cr	Ca	G	D	R	FS
details		4685-14-7	Paraquat	Ha	Cr	Ca	G	D	R	FS
details		2074-50-2	1,1'-Dimethyl-4,4'-bipyridinium bis(methyl sulfate)	Ha	Cr		G		R	FS

Paraquat via SuperToxic

SuperToxic

bioinf-services.charite.de/supertoxic/index.php?site=detail_view&ids=(27233)&path=

SuperToxic

Home

Toxin search

Structure search

Property search

Browse database

HowTo

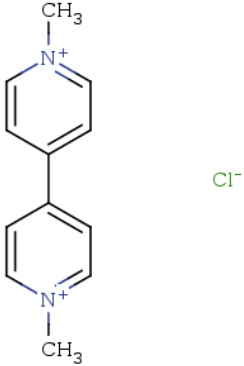
FAQ

Statistics

Contact

Links

Add a new compound

Information	Structure
<p>Synonyms:</p> <ul style="list-style-type: none">Bipyridinium, 1,1'-dimethyl-4,4'-, dichlorideDextrone-XGramixelGramoxoneGramoxone dichlorideGramoxone SGramoxone WMethyl viologenMethyl viologen (reduced)Methyl viologen dichlorideN,N'-Dimethyl-4,4'-bipyridinium dichlorideN,N'-Dimethyl-4,4'-bipyridylium dichlorideN,N'-Dimethyl-4,4'-dipyridylium dichlorideParaquatParaquat chlorideParaquat clParaquat dichlorideParaquat, dichlorideViologen, methyl-1,1-Dimethyl-4,4-dipyridilium dichloride1,1'-Dimethyl-4,4'-bipyridinium dichloride1,1'-Dimethyl-4,4'-bipyridinium dichloride1,1'-Dimethyl-4,4'-dipyridylium chloride1,1'-Dimethyl-4,4'-dipyridylium dichloride4,4'-Bipyridinium, 1,1'-dimethyl-, dichloride4,4'-Dimethyldipyridyl dichloride	
Smile:	<input type="text" value="[n+]1(ccc(cc1)c1cc[n+](cc1)C)[Cl-]"/>
Cas:	<input type="text" value="1910-42-5"/>
NSC:	<input type="text" value="263500"/>
Formula:	<input type="text" value="C12H14ClN2"/>
Rings:	<input type="text" value="2"/>
Atoms:	<input type="text" value="29"/>
Weight:	<input type="text" value="221.706"/>

CHARITÉ

Charité Berlin :: Structural Bioinformatics Group

Paraquat via CTD

Paraquat | CTD

ctdbase.org/detail.go?type=chem&acc=D010269

ctd Giving insight into how chemicals affect our health.

Comparative Toxicogenomics Database

Home Search Analyze Download Help

Paraquat

Basics Interactions Genes Diseases ChemComps Pathways GO References Links

Name Paraquat


CAS Type 1 Name 4,4'-Bipyridinium, 1,1'-dimethyl-

Equivalent Terms Gramoxone · Methyl Viologen · Paragreen A · Viologen, Methyl

CAS Registry Number 4685-14-7

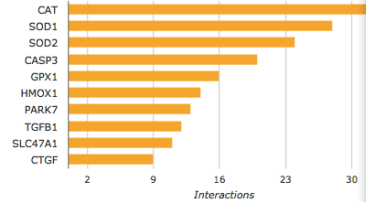
Definition A poisonous dipyridilium compound used as contact herbicide. Contact with concentrated solutions causes irritation of the skin, cracking and shedding of the nails, and delayed healing of cuts and wounds.

Chemical Drawing



MeSH ID D010269

Top Interacting Genes



Ancestors

Chemicals ← Heterocyclic Compounds ⇄ ← Heterocyclic Compounds, 1-Ring ⇄

Paraquat - Enriched Pathways | CTD

ctdbase.org/detail.go?type=chem&acc=D010269&view=pathway

ctd Giving insight into how chemicals affect our health.

Comparative Toxicogenomics Database

Home Search Analyze Download Help

Paraquat

Basics Interactions Genes Diseases ChemComps Pathways GO References Links

These pathways are enriched significantly among genes that interact with *Paraquat* or its descendants. We show only terms with a corrected p-value less than 0.01.

1-100 of 124 results.

Pathway	Pathway ID	P-value	Corrected P-value	Annotated Genes	Genome Frequency
1. Pathways in cancer	KEGG:05200	1.94e-48	5.30e-46	56	332/34620 genes: 0.96%
2. Signal Transduction	REACT:111102	1.55e-40	4.23e-38	94	1606/34620 genes: 4.64%
3. Metabolism	REACT:111217	1.61e-37	4.39e-35	83	1334/34620 genes: 3.85%
4. Chagas disease (American trypanosomiasis)	KEGG:05142	2.64e-35	7.22e-33	31	105/34620 genes: 0.30%
5. MAPK signaling pathway	KEGG:04010	6.02e-33	1.64e-30	41	281/34620 genes: 0.81%
6. Amyotrophic lateral sclerosis (ALS)	KEGG:05014	7.18e-31	1.96e-28	23	54/34620 genes: 0.16%
7. Tuberculosis	KEGG:05152	8.17e-30	2.23e-27	33	183/34620 genes: 0.53%
8. Immune System	REACT:6900	8.99e-30	2.45e-27	63	954/34620 genes: 2.76%
9. Osteoclast differentiation	KEGG:04380	5.74e-29	1.57e-26	29	132/34620 genes: 0.38%
10. Toxoplasmosis	KEGG:05145	1.16e-28	3.16e-26	29	135/34620 genes: 0.39%
11. Prostate cancer	KEGG:05215	8.39e-28	2.29e-25	25	91/34620 genes: 0.26%
12. Colorectal cancer	KEGG:05210	4.43e-27	1.21e-24	22	64/34620 genes: 0.18%
13. Pancreatic cancer	KEGG:05212	4.45e-26	1.22e-23	22	70/34620 genes: 0.20%
14. Disease	REACT:116125	2.95e-25	8.05e-23	49	667/34620 genes: 1.93%
15. Focal adhesion	KEGG:04510	3.05e-25	8.33e-23	31	211/34620 genes: 0.61%
16. Hemostasis	REACT:604	1.98e-24	5.39e-22	42	487/34620 genes: 1.41%
17. Cytokine-cytokine receptor interaction	KEGG:04060	8.15e-24	2.22e-21	33	277/34620 genes: 0.80%
18. Glutathione metabolism	KEGG:00480	8.76e-24	2.39e-21	19	54/34620 genes: 0.16%
19. Apoptosis	KEGG:04210	1.72e-23	4.69e-21	22	89/34620 genes: 0.26%
20. p53 signaling pathway	KEGG:04115	5.15e-23	1.41e-20	20	69/34620 genes: 0.20%
21. NOD-like receptor signaling pathway	KEGG:04621	1.03e-20	2.81e-18	18	63/34620 genes: 0.18%

Toxicology Databases

Other DBs

- General preference for breadth over depth
- Focus on toxicity, not molecular mechanisms
- Content is fragmented, limited search, not linked to other resources, lightly referenced

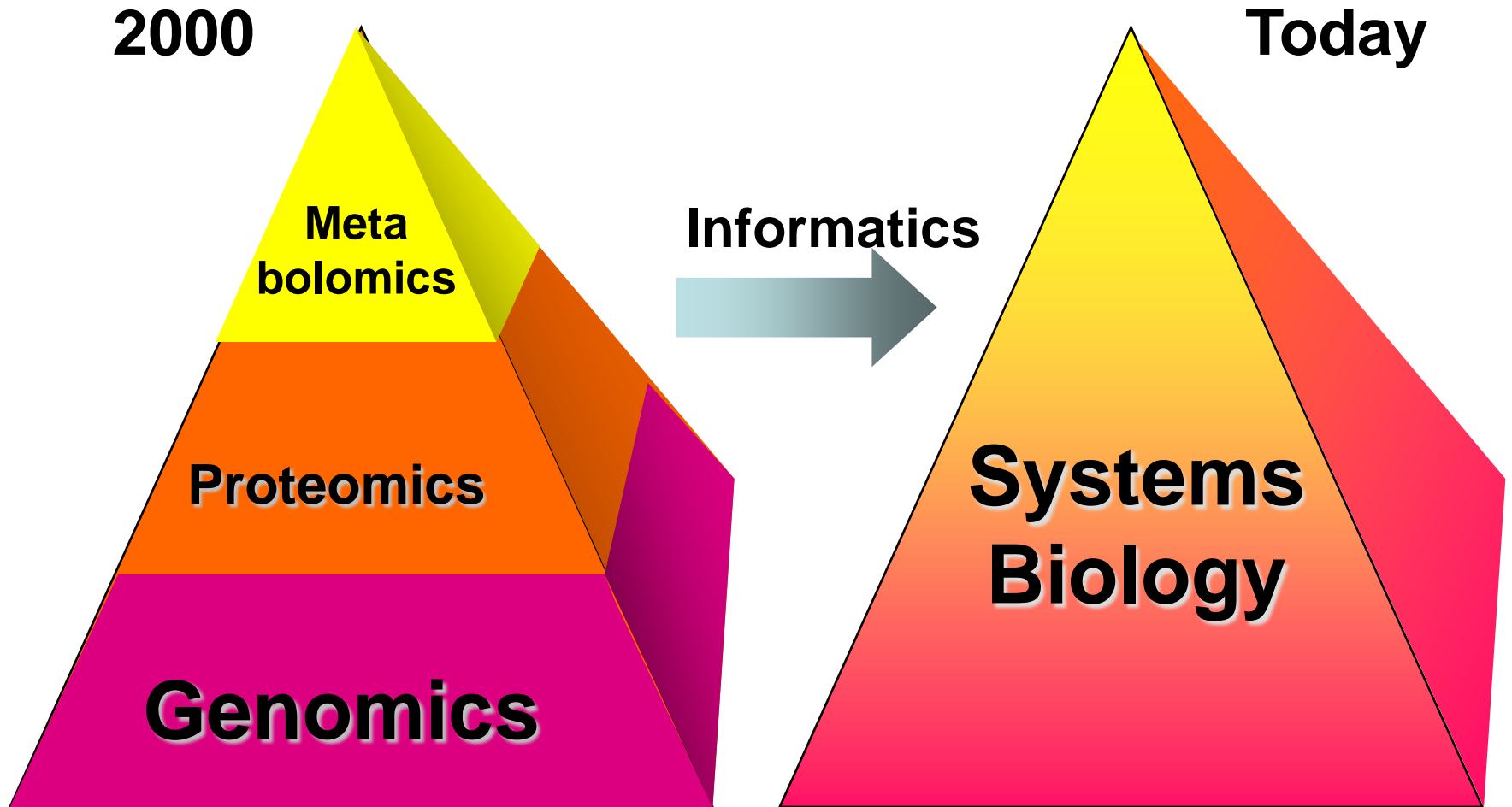
T3DB

- General reference for depth over breadth
- Focus on toxicity AND molecular mechanisms
- Content is uniform, extensive search offerings, linked to 15 other DBs, heavily referenced

Outline

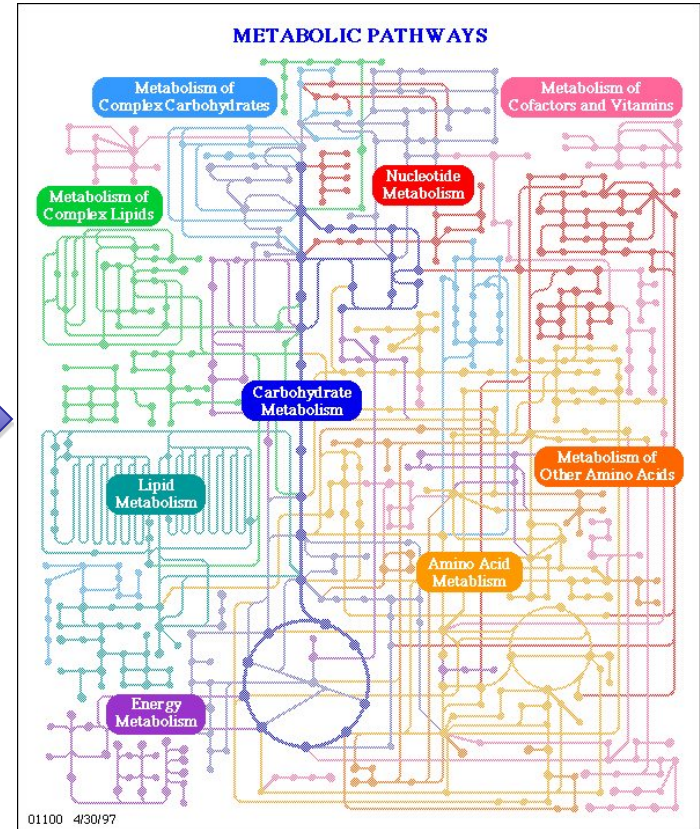
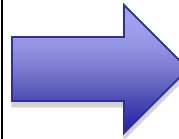
- **Brief review of toxicology databases**
- **Metabolomics and toxicology**
- **Introducing the toxin, toxin-target database – T3DB**
- **Systems biology, pathway databases and the small molecule database - SMPDB**
- **Conclusions & Future Directions**

Blurring the Borders



From Lists to Pathways

Compound	Retention Time (min)	Conc. in Urine (µM)	Compound	Retention Time (min)	Conc. in Urine (µM)
Dns-o-phospho -L-serine	0.92	<D.L. *	Dns-Ile	6.35	25
Dns-o-phospho -L-tyrosine	0.95	<D.L.	Dns-3-aminosalicylic acid	6.44	0.5
Dns -adenosine monophosphate	0.99	<D.L.	Dns-pipecolic acid	6.50	0.5
Dns-o-phosphoethanolamine	1.06	16	Dns-Leu	6.54	54
Dns-glucosamine	1.06	22	Dns-cystathionine	6.54	0.3
Dns-o-phospho -L-threonine	1.09	<D.L.	Dns-Leu-Pro	6.60	0.4
Dns-6-dimet hylamine purine	1.20	<D.L.	Dns-5-hydroxylysine	6.65	1.6
Dns-3-methyl -histidine	1.22	80	Dns-Cystine	6.73	160
Dns-taurine	1.25	834	Dns-N-norleucine	6.81	0.1
Dns-carnosine	1.34	28	Dns-5-hydroxydopamine	7.17	<D.L.
Dns-Arg	1.53	36	Dns-dimethylamine	7.33	293
Dns-Asn	1.55	133	Dns-5-HIAA	7.46	18
Dns-hypotaurine	1.58	10	Dns-umbelliferone	7.47	1.9
Dns-homocarnosine	1.61	3.9	Dns-2,3-diaminoproprionic acid	7.63	<D.L.
Dns-guanidine	1.62	<D.L.	Dns-L-ornithine	7.70	15
Dns-Gln	1.72	633	Dns-4-acetyamidophenol	7.73	51
Dns-allantoin	1.83	3.8	Dns-procaine	7.73	8.9
Dns-L-citrulline	1.87	2.9	Dns-homocystine	7.76	3.3
Dns-1 (or 3 -)-methylhistamine	1.94	1.9	Dns-acetaminophen	7.97	82
Dns-adenosine	2.06	2.6	Dns-Phe-Phe	8.03	0.4
Dns-methylguanidine	2.20	<D.L.	Dns-5-methoxy salicylic acid	8.04	2.1
Dns-Ser	2.24	511	Dns-Lys	8.16	184
Dns-aspartic acid amide	2.44	26	Dns-aniline	8.17	<D.L.
Dns-4-hydroxy -proline	2.56	2.3	Dns-leu-Phe	8.22	0.3
Dns-Glu	2.57	21	Dns-His	8.35	1550
Dns-Asp	2.60	90	Dns-4-thialysine	8.37	<D.L.
Dns-Thr	3.03	157	Dns-benzylamine	8.38	<D.L.
Dns-epinephrine	3.05	<D.L.	Dns-1-ephedrine	8.50	0.6
Dns-ethanolamine	3.11	471	Dns-tryptamine	8.63	0.4
Dns-aminoadipic acid	3.17	70	Dns-pyridoxamine	8.94	<D.L.
Dns-Gly	3.43	2510	Dns-2-methyl -benzylamine	9.24	<D.L.
Dns-Ala	3.88	593	Dns-5-hydroxytryptophan	9.25	0.12
Dns-aminolevulinic acid	3.97	30	Dns-1,3-diaminopropane	9.44	0.23
Dns-r-amino -butyric acid	3.98	4.6	Dns-putrescine	9.60	0.5
Dns-p-amino -hippuric acid	3.98	2.9	Dns-1,2-diaminopropane	9.66	0.1
Dns-5-hydroxymethyluricil	4.58	1.9	Dns-tyrosinamide	9.79	29
Dns-tryptophanamide	4.70	5.5	Dns-dopamine	10.08	140
Dns-isoguanine	4.75	<D.L.	Dns-cadaverine	10.08	0.08
Dns-5-aminopentanoic acid	4.79	1.6	Dns-histamine	10.19	0.4
Dns-sarcosine	4.81	7.2	Dns-3-methoxy -tyr amine	10.19	9.2
Dns-3-amino -isobutyrate	4.81	85	Dns-Tyr	10.28	321
Dns-2-aminobutyric acid	4.91	17	Dns-cysteamine	10.44	<D.L.



Pathway DBs

KEGG

UniPathway

BioCyc/MetaCyc

Reactome

Current Pathway DBs

- **Most are multi-organism in nature without emphasis on humans**
- **Most have very simple diagrams with no visible indication of cellular compartments or visible protein/chemical structure**
- **Most focus on regular metabolism, not diseases, drugs, toxins or poisons**
- **Most focus on cellular processes, not whole organisms or multi-organ processes**

The Small Molecule Pathway Database (SMPDB)

The image shows two browser windows. The top window is the SMPDB Home page, which includes a search bar and a welcome message. The bottom window shows a search result for '17-Beta Hydroxysteroid Dehydrogenase III Deficiency'. The result includes a pathway diagram, a description of the disease, and a list of associated metabolites and enzymes.

17-Beta Hydroxysteroid Dehydrogenase III Deficiency

Defects in 17-beta hydroxysteroid dehydrogenase III (HSD17B3) are the cause of male pseudohermaphroditism with gynecomastia. These individuals have unambiguous female external genitalia at birth, but fail to menstruate at the time of expected puberty and instead virilize as evidenced by growth (more)

2-Hydroxyglutaric Aciduria (D And L Form)

L-2-Hydroxyglutaric Aciduria(D-2-Hydroxyglutaric Aciduria) is an autosomal recessive disease caused by a mutation in the L2HGDH gene which codes for L-2-Hydroxyglutarate dehydrogenase. A deficiency in this enzyme results in accumulation of L-2-Hydroxyglutaric acid in plasma, spinal fluid, and (more)

3-Methyl-3-Hydroxybutyl CoA Dehydrogenase Deficiency

3-Methyl-3-hydroxybutyl CoA dehydrogenase deficiency(Hydroxyl-CoA dehydrogenase deficiency)

<http://www.smpdb.ca>

- >450 small molecule pathways for Humans ONLY
- 223 drug/toxin pathways
- 116 disease pathways
- 13 signalling pathways
- 90 metabolic pathways
- Depicts cell compartments, organelles, protein locations, 4^o structures
- Maps genechip & metabolomic data
- Converts gene, protein or chemical lists to pathways or disease diagnoses

Inside SMPDB

Phenylketonuria

<http://129.128.246.213/pathman/pathways/SMP00206/pathway>

Audiobaba Music Search Bioinformati... the U of A! Coilgun Basics 2 Pathguide: t...source list Dictionary o...n.ca: Books Lipid Analys...s Fiehn Lab Metabolomic...n's Disease Statistical Tests

Phenylketonuria (Hyperphenylalaninemia ; HPA ; PKU) is an autosomal recessive genetic disorder characterized by a deficiency in the enzyme hepatic phenylalanine hydroxylase (PAH). PAH is necessary to metabolize the amino acid phenylalanine to the amino acid tyrosine. When PAH is deficient, phenylalanine accumulates and is converted into phenylpyruvate, which is detected in the urine. Left untreated, this condition can cause problems with brain development, leading to progressive mental retardation and seizures.

Component Index

Hide Index

Metabolites:

- 4-Fumarylacetoacetic acid
- 4-Hydroxyphenylpyruvic acid
- Acetoacetic acid
- Ammonia
- Fumaric acid
- Homogentisic acid
- Hydrogen peroxide
- L-Phenylalanine
- L-Tyrosine
- Malesylacetoacetic acid
- Oxygen
- Phenylpyruvic acid
- Water

Enzymes:

- 4-hydroxyphenylpyruvate dioxygenase
- Aspartate aminotransferase, cytoplasmic
- Fumarylacetoacetase
- Homogentisate 1,2-dioxygenase
- Kunitz chymotrypsin inhibitor 2
- L-amino-acid oxidase
- Phenylalanine-4-hydroxylase
- Phenylalanyl-tRNA synthetase alpha chain
- Phenylalanyl-tRNA synthetase beta chain
- Tyrosine aminotransferase
- Tyrosyl-tRNA synthetase, cytoplasmic

Pathway Legend

Zoom In

Phenylketonuria In *Homo sapiens*

Metabolite Legend:

- Phenylalanine
- Tyrosine
- Phenylpyruvate
- 4-Hydroxyphenylpyruvate
- 4-Fumarylacetoacetic acid

Enzyme Legend:

- Phenylalanine hydroxylase (PAH)
- Phenylpyruvate transferase (PPTase)
- 4-Hydroxyphenylpyruvate dioxygenase
- Fumarylacetoacetase

Enzyme Details (from popup):

Phenylalanine hydroxylase (PAH)

Protein name: Phenylalanine hydroxylase (EC 1.1.1.1)

EC number: EC 1.1.1.1

Alternative names: L-phenylalanine aminohydroxylase

Gene name: PAH

Organism: Homo sapiens (Human) (Comptes rendus)

Taxonomic identifier: 9606 (NCBI)

Taxonomic lineage: Eukaryota; Metazoa; Chordata; Chordata Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontiformes; Primates; Haplorhini; Catarrhini; Hominoidea; Hominidae

Protein attributes:

- Sequence length: 501 AA
- Sequence status: Complete
- Reference proteomics: The UniProt database is not processed.
- Protein existence: Evidence at protein level.

Catalytic activity: L-tyrosine + 2-oxoglutarate + 4-hydroxyphenylpyruvate + L-glutamate

EC number: EC 1.1.1.1

Pathway description: Amino-acid dependent L-phenylalanine hydroxylation; aspartic acid and fumarate form L-phenylalanine step 25.

Subunit structure: Monomeric (1:1:1:1)

Involvement in disease: Defects in PAH are the cause of phenylketonuria type II (PKU2) [MIM:263000] also known as BH4-deficient phenylketonuria. Pathway is not shown in detail.

Mapping Metabolites with SMPDB

The screenshot shows the SMPDB website home page. At the top, there is a navigation bar with links for Home, Browse, Search, About, Downloads, and Contact Us. Below this is a search bar with the text "Search: Search SMPDB" and a "Search" button. Underneath the search bar, it says "SMP-MAP" and "Search by: Metabolite Name" with a "Go" button. A section titled "Search by metabolite name" contains a text input field with the text "phenylalanine, pyruvic acid, tyrosine, phenylacetate, phenylacetate." and a "Search" button. Below this, there is an example: "Example: L-Arginine, Geranylgeranyl-PP, Geranyl-PP" and another "Search" button. At the bottom of the page, there is a small text block: "This project is supported by Genome Alberta & Genome Canada, a not-for-profit organization that is leading Canada's national genomics strategy with \$600 million in funding from the federal government."

The screenshot shows a detailed metabolic pathway map for Citrullinemia Type I. The map is set against a background of a liver cross-section. The pathway is represented by a network of nodes (metabolites) and arrows (enzymes). Key nodes include Citrulline, Ornithine, L-Arginine, L-Aspartic acid, L-Glutamic acid, L-Glutamine, L-Lysine, Omithine, Oxalacetic acid, Oxoglutaric acid, Pyruvic acid, Urea, and Water. The pathway is color-coded, with yellow nodes and arrows indicating the primary pathway and red nodes and arrows indicating secondary or related pathways. A legend on the right side of the page lists the metabolites and proteins involved in the pathway, with checkboxes next to each item. The legend is divided into two sections: "Metabolites" and "Proteins". The "Metabolites" section lists 15 items, with checkboxes for Adenosine monophosphate, Adenosine triphosphate, ADP, Ammonia, Argininosuccinic acid, Carbamoylphosphate, Citrulline, Fumaric acid, Hydrogen carbonate, L-Alanine, L-Arginine, L-Aspartic acid, L-Glutamic acid, L-Glutamine, L-Lysine, Omithine, Oxalacetic acid, Oxoglutaric acid, Pyruvic acid, Urea, and Water. The "Proteins" section lists 7 items, with checkboxes for Alanine aminotransferase 1, Arginase-1, Argininosuccinate lyase, Argininosuccinate synthase, Aspartate aminotransferase, mitochondrial, Carbamoyl-phosphate synthase [ammonia], mitochondrial, and Glutamate dehydrogenase 1, mitochondrial. The status bar at the bottom of the page reads: "Loading 'http://129.128.246.213/pathman/pathways/SMP00001/pathway', completed 27 of 28 items".

SMPDB

- **Original SMPDB images were hand-drawn and not easily manipulated or updated, pathways were non-computable and not stored in ML compliant file structure**
- **Now going through a major update to save all files in BioPax format (which can be converted to SBML)**
- **Also creating a drawing widget that allows everyone to quickly create nicely colored, BioPax compatible SMPDB pathways**
- **Still hundreds of pathways to add....**

Conclusion

- **Current toxicology/toxicity databases are not yet oriented to systems or predictive toxicology**
- **Emerging resources (ToxcastDB, ToxBank Wiki, T3DB) are starting to change this**
- **T3DB is still a work in progress**
- **Current pathway databases still not oriented to toxicology, they are still missing key information**
- **SMPDB is a step in the right direction, but not yet “finished”**
- **Still plenty of work to do and plenty of opportunities to share/exchange data**

Thanks To

- **Staff** - Rupasri Mandal, Ram Krishnamurthy, Farid Aziat, Edison Dong, Igor Sinelnikov, Jeff Xia, Kruti Chaudhary, Souhaila Bouatra, Nick Psychogios, Trent Bjorndahl, Rolando Perez-Pinero, **Mike Wilson, Craig Knox, Zerihun Dame, Philip Liu, Faizath Yallou, An Chi Guo, Yifeng Liu, You Zhou, Tim Jewison, Vanessa Neveu, Yannick Djoumbou, David Arndt**
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- **Collaborators** - Liang Li, Christoph Borchers, Russ Greiner, Augustin Scalbert
- **Funders** - CIHR, Genome Canada, AIBS, NSERC