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Abstract Sifter: A literature informatics tool for chemical safety assessments

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Introduction

By the year 2035, the US EPA aims to eliminate animal testing in chemical safety assessment by adopting a set of new approach methods (NAMs). These methods will rely on rich data and an understanding of the mechanisms underpinning chemical toxicity. The biomedical literature is a rich source of information about mechanisms of toxicity, but because resources like PubMed are so large and complex, literature informatics methods are needed to help researchers use this resource more effectively.

We have developed a freely available Excel-based literature tool called the Abstract Sifter to retrieve and triage articles and to visualize the literature landscape for a set of chemicals¹. The tool is with queries that facilitate exploration of mechanistic information by using the language of Adverse Outcome Pathways (AOPs) and Key Characteristics of Carcinogens².

Defining mechanisms through PubMed queries

Toxicity type queries

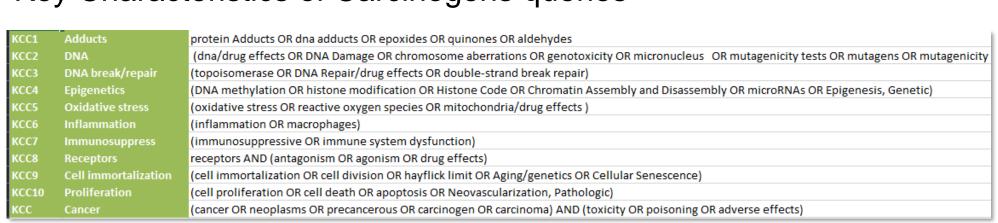
Genetox	(dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR DNA Repair OR mutagenicity to
Cancer	neoplasms or cancer
ReproTox	(reproduction AND (toxicity OR abnormal OR adverse effects))
NeuroTox	(neurotoxicity OR (Nervous system diseases and chemically induced) OR ((neurons OR brain OR behavior) AND drug effects)
DevTox	(toxicity OR congenital abnormalities OR Prenatal Exposure Delayed Effects) AND (fetus OR embryo OR embryonic development)
Skin sensitization	("allergic" AND "contact" And dermatitis) OR Dermatitis, Allergic Contact[mh]

AMP augries

AOP queries		Events: Molecular Initiating Events (MIE) 🗿 Key Events (KE) 💿 Adverse Outcomes (AO) 🗿						
, , ,	940		Sequence	Туре	Event ID	Title	Short name	
			1	MIE	305	Inhibition, VegfR2	Inhibition, VegfR2	
aop43	1mie	(Vascular Endothelial Growth Factor Receptor-2 OR Vascular Endothelial Growth Facto						
aop43	2ke	((angiogenesis OR vasculogenesis) AND (reduce OR inhibit)) OR (Neovascularization, I	2	KE	28	Reduction, Angiogenesis	Reduction, Angiogenesis	
aop43	3ke	endothelium OR endothelial AND (damage OR impair OR impairment)	3	KE	110	Impairment, Endothelial network	Impairment, Endothelial network	
aop44	4ke	Blood circulation AND (drug effects AND toxicity)	4	KE	298	Insufficiency, Vascular	Insufficiency, Vascular	
aop43	5ao1	birth defects OR Congenital Abnormalities	5	AO	1001	Increased, Developmental Defects	Increased, Developmental Defects	
aop43	6ao2	(bone OR bone development OR calcification OR osteogenesis OR limb bud/drug effection)				And jemonyo on emon	ome acreiopment	
		A constitution of						

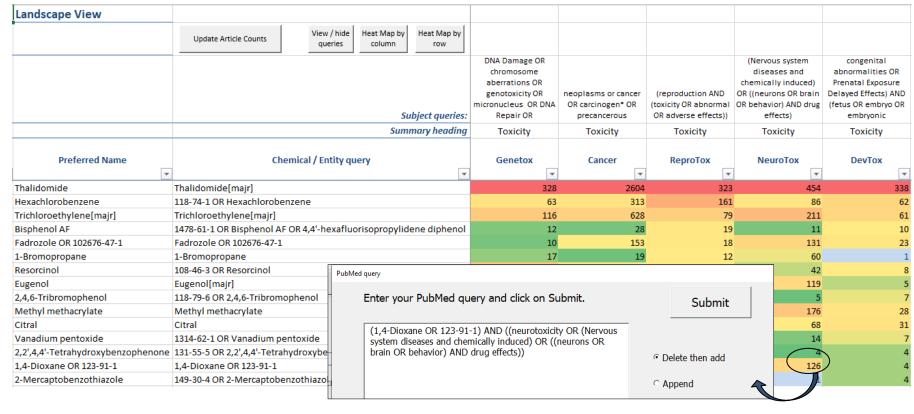
Aopwiki.org

Key Characteristics of Carcinogens queries



Landscape Overview

The Landscape an overview of a literature domain by entering entity and subject matter queries.



Toxicity Types

The numbers are article counts retrieved by the application. Double-clicking on the article count retrieves the citations and sends them to the Main

To sift, enter terms or characters of interest here and let the Abstract Sifter count occurrences of the terms in the title and abstract. Then sort. Doubleclicking on a row sends the user to the Abstract sheet

Retrieve and sift the citations

The Main sheet is where the user can browse and use the novel sifting technology to find relevant articles

> What other things can you do?

terms colorized

for easy

reading.

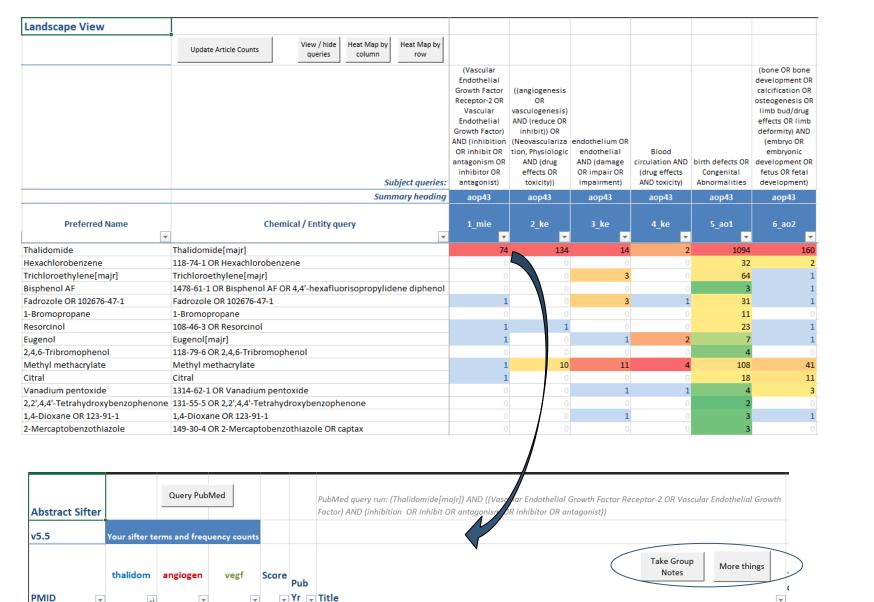
The Notes sheet offers other usefu capabilities



was determined at 640 ppm for both rats and mice, since the nuclear enlargement in the nasal respiratory epithelium and the centrilobular swelling of hepatocytes in rats and the nuclear enlargement in the bronchial epithelium in mice were observed at 1,600 ppm. The NOAEL value corresponded to the estimated 1,4-dioxane intake of 52 mg/kg/day in rats and 170 mg/kg/day in mice. KEYWORDS: Dioxanes, Solvents, 1,4-dioxane, Administration, Oral, Animals, Dioxanes/toxicity, Female, Liver/drug effects/growth & development/pathology, Male, Mice, No-Observed-Adverse-Effect Level, Organ Size, Rats, Rats, Inbred F344, Respiratory System/drug effects/growth & development/pathology, Solvents/toxicity

AOP 43: Vascular disruption

Landscape view for three sample mechanistic reviews



2009 [Inhibitory effect of thalidomide on growth of human hepatoma cell line SMMC-7721 cells]. 2005 Thalidomide inhibits growth of tumors through COX-2 degradation independent of antiangiogenesis.

2019 Immunomodulatory drugs alleviate I-dopa-induced dyskinesia in a rat model of Parkinson's disease.

2014 In vitro anti-proliferative and anti-angiogenic activities of thalidomide dithiocarbamate analog

2002 Renal cell carcinoma may adapt to and overcome anti-angiogenic intervention with thalidomid 1999 Thalidomide and a thalidomide analogue inhibit endothelial cell proliferation in vitro.

14 2015 [Inhibitory effect of thalidomide combined with interferon on the proliferation of Kasumi-1 cells].

2004 Antitumor effects of thalidomide analogs in human prostate cancer xenografts implanted in immunodeficient mic

2010 Thalidomide inhibits inflammatory and angiogenic activation of human intestinal microvascular endothelial cells (HIMFC

2005 Thalidomide-induced antiangiogenic action is mediated by ceramide through depletion of VEGF receptors, and is antagonized

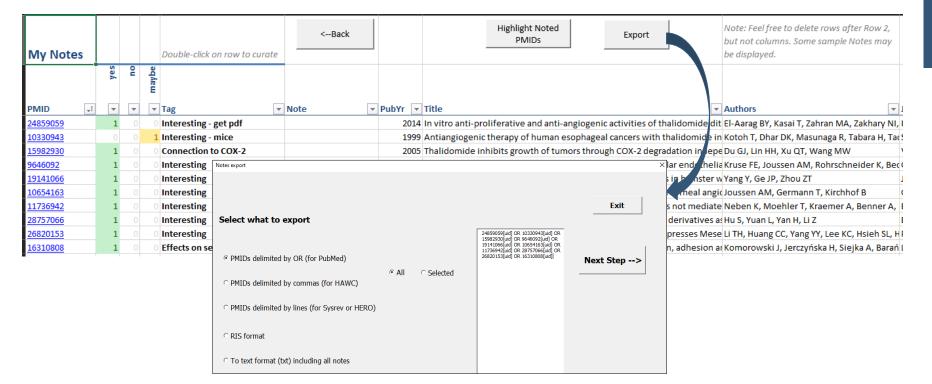
5 2017 Anticancer effects of novel thalidomide analogs in A549 cells through inhibition of vascular endothelial growth factor and mat

2006 Effect of thalidomide affecting VEGF secretion, cell migration, adhesion and capillary tube formation of human endothelial EA.h

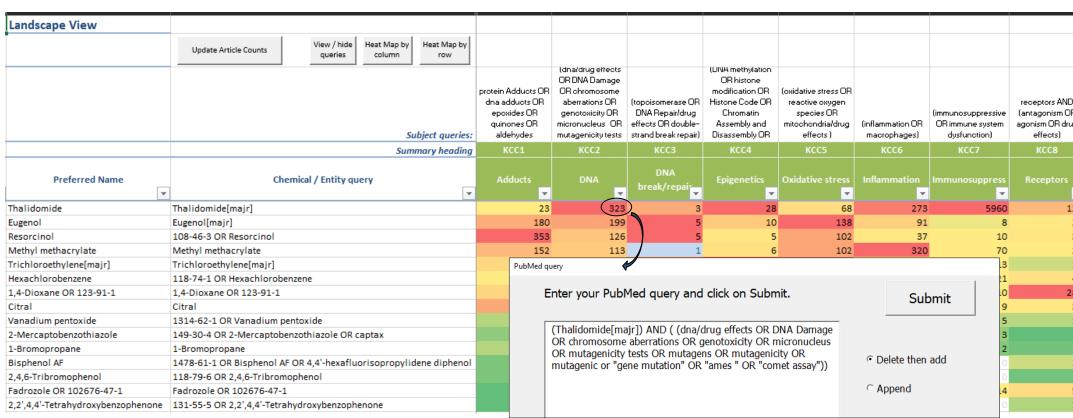
15 2013 The suppression effects of thalidomide on human lung fibroblasts: cell proliferation, vascular endothelial growth factor relea:

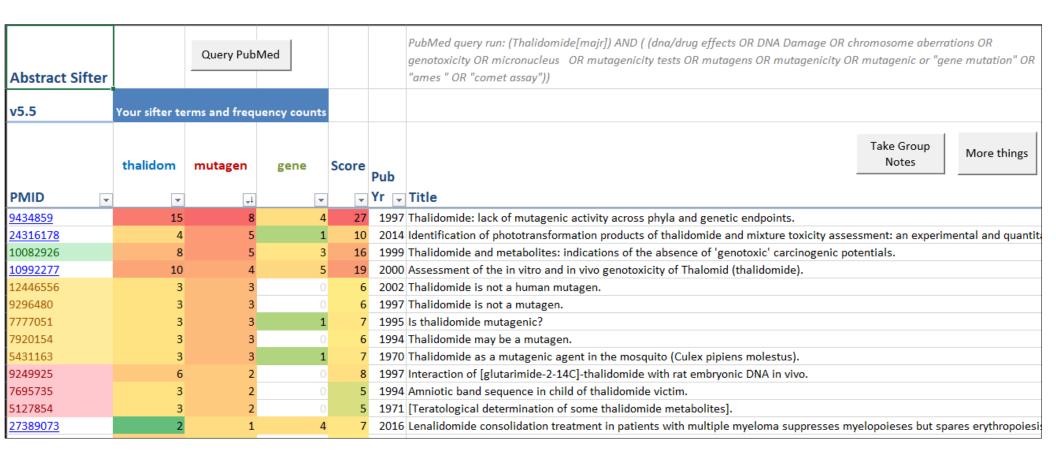
1 13 2008 Thalidomide inhibits epidermal growth factor-induced cell growth in mouse and human monocytic leukemia cells via Ras inactiv

Citations on the Notes sheet can be exported to other software.



Key Characteristics of Carcinogens





Notes can be taken and noted articles highlighted.

Summary

The Abstract Sifter is a free, innovative tool that provides an effective way to retrieve, read, tag, filter and export PubMed citations. The tool additionally offers an overview of a complex literature landscape for lists of chemicals and the capability of focusing on details of chemical activity such as mechanisms of toxicity or adverse outcome pathways. The Abstract Sifter is downloadable here: https://comptox.epa.gov/dashboard/downloads and a hands-on training is available on October 23 through the ASCCT meeting.

References: 1) Baker N et al. F1000 Res. 2017 Dec 21;6. pii: Chem Inf Sci-2164. 2) Smith, et al. Environ Health Perspect. 2016 Jun;124(6):713-21.