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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 chemicals<sup>1</sup>. The tool is supplied with queries that facilitate exploration of mechanistic information by using the language of Adverse Outcome Pathways (AOPs) and Key Characteristics of Carcinogens<sup>2</sup>.

## Toxicity type queries

## AOP queries

Aopwiki.org

## Key Characteristics of Carcinogens queries

KCC2	Adducts	protein Adducts OR dna adducts OR epoxides OR quinones OR aldehydes
KCC2	DNA	(dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR mutagenicity tests OR mutagens OR mutagenicity (topoisomerase OR DNA Repair/drug effects OR double-strand break repair)
KCC3	DNA break/repair	(DNA methylation OR histone modification OR Histone Code OR Chromatin Assembly and Disassembly OR microRNAs OR Epigenesis, Genetic)
KCC4	Epigenetics	(oxidative stress OR reactive oxygen species OR mitochondria/drug effects)
KCC5	Oxidative stress	(inflammation OR macrophages)
KCC6	Inflammation	(immunosuppressive OR immune system dysfunction)
KCC7	Immunosuppress	receptors AND (antagonism OR agonism OR drug effects)
KCC8	Receptors	(cell immortalization OR cell division OR hayflick limit OR Aging/genetics OR Cellular Senescence)
KCC9	Cell immortalization	(cell proliferation OR cell death OR apoptosis OR Neovascularization, Pathologic)
KCC10	Proliferation	(cancer OR neoplasms OR precancerous OR carcinogen OR carcinoma) AND (toxicity OR poisoning OR adverse effects)
KCC	Cancer	

**U.S. Environmental Protection Agency**  
Office of Research and Development

*This poster does not necessarily represent U.S. EPA policy.*

## Toxicity Types

[illegible]

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

*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. Double-clicking 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?

The Notes sheet offers other useful capabilities.

## AOP 43: Vascular disruption

Landscape View		Update Article Counts	View / Hide queries	Heat Map by column	Heat Map by row										
						(Vascular Endothelial Growth Factor Receptor-2 OR Vascular Endothelial Growth Factor AND Inhibition) AND (angiogenesis OR angiogenesis OR									

Abstract Strct		PubMed query (thalidomide[mg]) AND (Pro- or Endothelial Growth Factor Receptor-2 OR Vascular Endothelial Growth Factor) AND (Inhibition OR inhibits OR antagonizes OR inhibitor OR antagonist)									
v5.5	Your filter terms and frequency counts										
	thalidom	angigen	veg	score	Pub	Take Group Notes		More things			
PMID	thalidom	angigen	veg	score	Pub						
20021944	15	3	3	21	2009	Inhibitory effect of thalidomide on growth of human hepatoma cell lines SMMC-7721 cells.					
15989390	14	6	2	24	2010	Thalidomide inhibits growth of tumors through COX-2 degradation and attenuation of angiogenesis.					
15989390	14	6	2	24	2010	Antitumor effects of thalidomide analogs in human prostate cancer xenografts implanted in immunodeficient mice.					
15989390	14	6	2	24	2010	Immunomodulatory drugs elicit a dose-induced dysregulation in a rat model of Parkinson's disease.					
16465764	13	6	10	20	2010	Thalidomide angiogenic activity is attenuated by inhibition of endothelial nitric oxide synthase.					
16465764	13	6	10	20	2010	Chronic thalidomide administration enhances vascular responsiveness to vasopressin in portal-systemic alterations of bile duct obstruction.					
16829128	12	5	10	2018	Thalidomide Improves Psoasitis-like Lesions and Reduces Tactile Allodynia in VEGF Expression without Alteration of Microvessel Density in Experimental Psoriasis.						
24850959	13	1	10	2014	Effects of Thalidomide Combined with Interferon on Inhibiting Kaposi's Sarcoma Cell Proliferation.						
24850959	12	11	4	2014	In vitro pro-angiogenic and anti-angiogenic activities of thalidomide dithiocarbamate analogs.						
15424122	12	4	20	2005	Thalidomide-induced antiangiogenic action is mediated by ceramide through down-regulation of VEGFR receptors, and is antagonized by sphingosine.						
15424122	12	4	20	2005	Thalidomide for the treatment of multiple myeloma.						
11842020	12	6	18	2002	Renal cell carcinoma may act to and overcome anti-angiogenic intervention with thalidomide.						
10532772	12	6	15	1999	Thalidomide and a thalidomide analogue inhibit endothelial cell proliferation <i>in vitro</i> .						
15216483	12	6	15	2017	Anticancer effects of thalidomide analogs in A549 cells through inhibition of vascular endothelial growth factor and matrix metalloproteinase-2.						
26803553	12	4	24	2016	Thalidomide Improves the Intestinal Mucosal Injury and Suppresses Mesenteric Angiogenesis and Vasodilatation by Down-Regulating the Endothelial Nitric Oxide Synthase.						
15216483	12	6	15	2016	Thalidomide as an immunotherapeutic agent: the effects on macrophil-mediated angiogenesis.						
16466772	12	4	24	2015	Inhibitory effect of thalidomide combined with interferon on the proliferation of Kasumi-1 cells.						
22722461	10	4	15	2013	The suppression effects of thalidomide on human lung fibroblasts: cell proliferation, vascular endothelial growth factor release, and angiogenesis.						
22722461	10	4	15	2018	Thalidomide inhibits thalidomide growth factor-induced cell growth in response and human umbilical vein endothelial cells via Ras/Rac1 pathway.						
61368008	10	7	5	2006	Effect of thalidomide on VEGF secretion, cell migration, adhesion and capillary tube formation of human endothelial EA.hy926 cells.						

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

The screenshot shows the PubMed search results page. At the top, there is a search bar with the text "Thalidomide inhibits growth of tumors through COX-2 degradation". Below the search bar, there is a table of search results. The table has columns for "PMID", "Title", "Author", and "Year". The first three results are highlighted in yellow. The first result is "Thalidomide inhibits growth of tumors through COX-2 degradation" by Zhang et al. (2005). The second result is "Thalidomide inhibits growth of tumors through COX-2 degradation" by Zhang et al. (2005). The third result is "Thalidomide inhibits growth of tumors through COX-2 degradation" by Zhang et al. (2005). To the right of the table, there is a "Next Step" button. Below the table, there is a section for "Selected what to export" with options for "PMIDs delimited by OR (for PubMed)", "PMIDs delimited by commas (for HANIC)", "PMIDs delimited by lines (for Sysrev or HERO)", "RIS format", and "To text format (txt) including all notes".

PMID	Title	Author	Year
24879059	Interesting: get pdf	2014 In vitro anti-proliferative and anti-angiogenic activities of thalidomide	2014
10010942	Interesting: nice	1999 Antitumor activity of thalidomide in human esophageal cancer	1999
19562939	Interesting: to COX-2	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
9645992	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
3111066	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
10064163	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
11216462	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
28727066	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
26820153	Interesting	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005
16311888	Effects on	2005 Thalidomide inhibits growth of tumors through COX-2 degradation	2005

Selected what to export

- ☐ PMIDs delimited by OR (for PubMed)
- ☐ PMIDs delimited by commas (for HANIC)
- ☐ PMIDs delimited by lines (for Sysrev or HERO)
- ☐ RIS format
- ☐ To text format (txt) including all notes

Next Step ->

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.

## Key Characteristics of Carcinogens

[illegible]

Abstract Sifter		Query PubMed		PubMed query run (Thalidomide[majr]) AND ( (dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR mutagenicity tests OR mutagens OR mutagenicity OR mutagenic OR "gene mutation" OR "ames" OR "comet assay") )	
v5.5	Your sifter terms and frequency counts				
	thalidom	mutagen	gene	Score	Pub
PMID					Title
9434859	15	8	4	27	1997 Thalidomide: lack of mutagenic activity across phyla and genetic endpoints.
24316178	4	5	1	10	2014 Identification of transformation products of thalidomide and mixture toxicity assessment: an experimental and quantitative approach.
10082926	8	5	3	16	1999 Thalidomide and metabolites: indications of the absence of 'genotoxic' carcinogenic potentials.
20992272	10	4	5	19	2000 Assessment of the in vitro and in vivo genotoxicity of Thalomid (thalidomide).
12446556	3	3	0	6	2002 Thalidomide is not a human mutagen.
9296480	3	3	0	6	1997 Thalidomide is not a mutagen.
7777051	3	3	1	7	1995 Is thalidomide mutagenic?
7920154	3	3	0	6	2014 Thalidomide may be a mutagen.
5431163	3	3	1	7	1970 Thalidomide as a mutagenic agent in the mosquito (Culex pipiens molestus).
92498325	6	2	0	8	1997 Interaction of [glutamine-2,4-C <sup>14</sup> ] thalidomide with rat embryonic DNA in vivo.
7695735	3	2	0	5	1994 Amniotic band sequence in child of thalidomide victim.
5127854	3	2	0	5	1971 [Teratological determination of some thalidomide metabolites].
27389073	2	1	4	7	2016 Lenalidomide consolidation treatment in patients with multiple myeloma suppresses myelopoieses but spares erythropoiesis.

*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.