Prioritizing Chemical Agents for Cancer Hazard Identification

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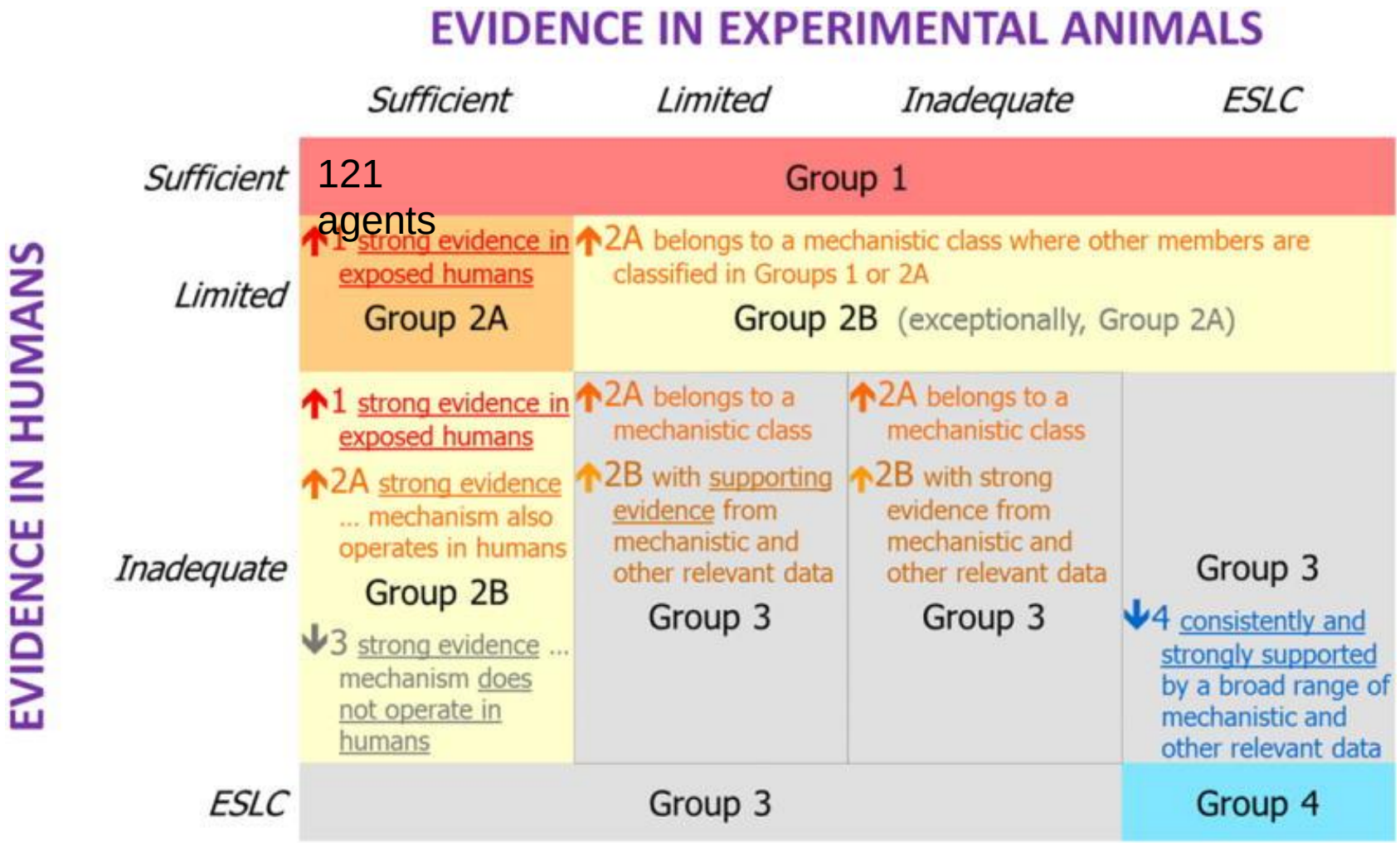
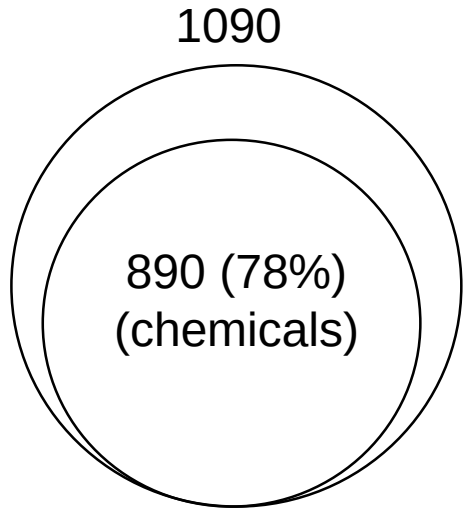
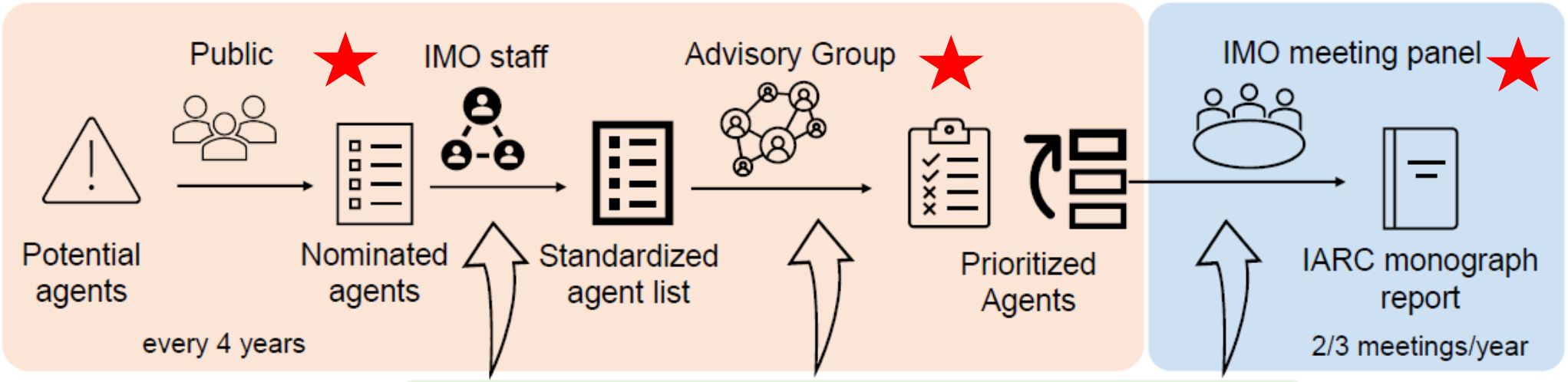
IARC Monographs – the encyclopedia of carcinogenic agents





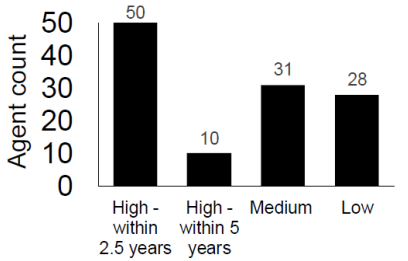
Source : PMC5783793

Cancer hazard identification process



33 millions papers (PubMed)

110 millions chemicals (PubChem)

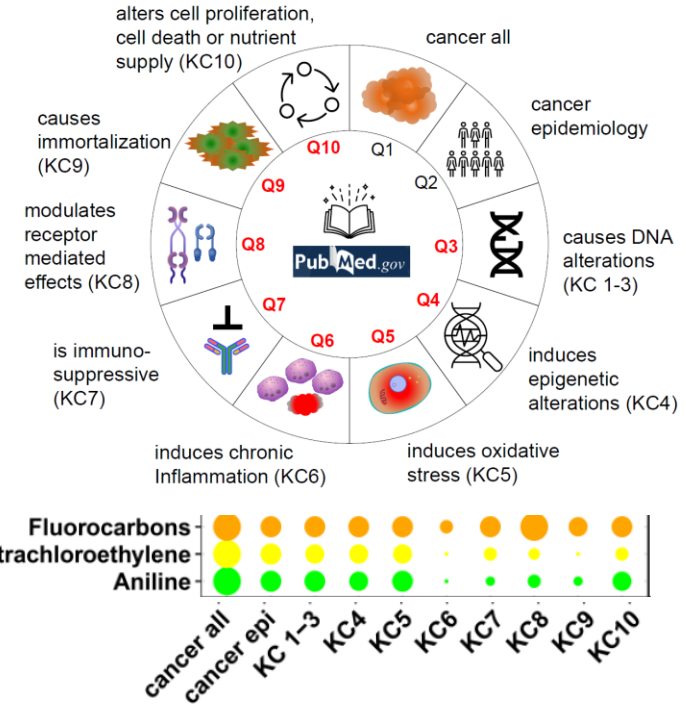


Need to develop new **computational approaches** to utilize **literature and chemical databases** for the cancer hazard identification process.

Which chemical agents should be nominated and evaluated ? → Chemical prioritization

How to prioritize chemical agents ?

Chemical text mining



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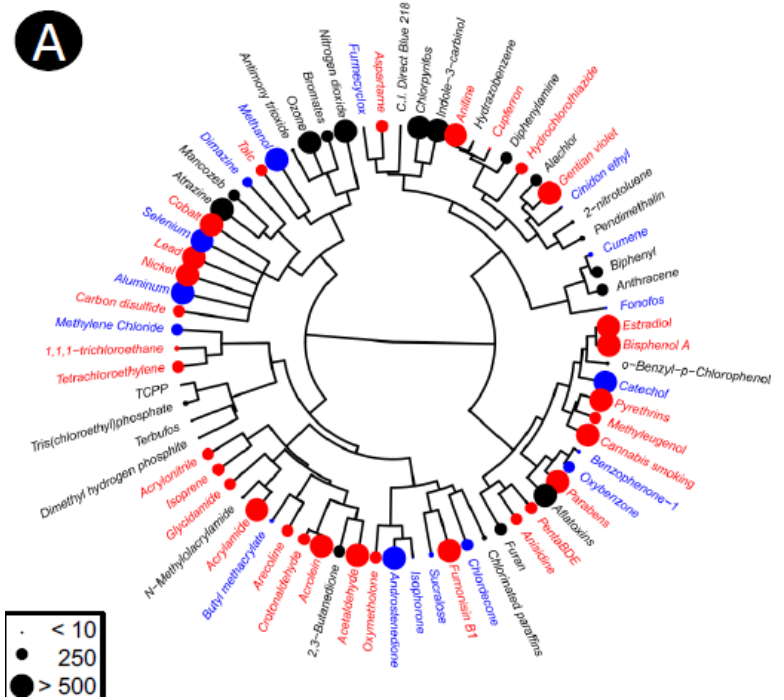
Chemoinformatics



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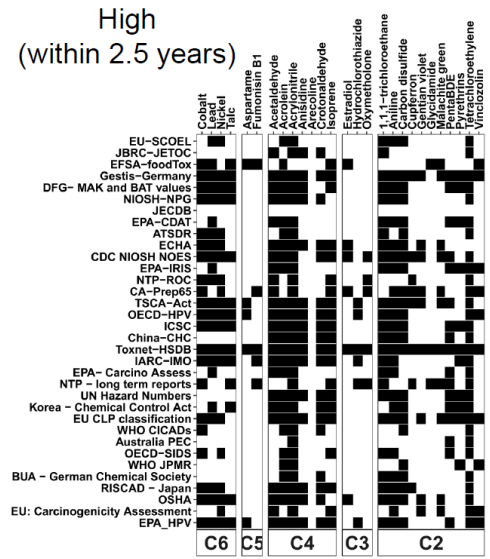
Database fusion



1. Barupal, Dinesh Kumar, Mary K. Schubauer-Berigan, Michael Korenjak, Jiri Zavadil, and Kathryn Z. Guyton. "Prioritizing cancer hazard assessments for IARC Monographs using an integrated approach of database fusion and text mining." *Environment International* 156 (2021): 106624.
2. Guha, N., Guyton, K. Z., Loomis, D., & Barupal, D. K. (2016). Prioritizing chemicals for risk assessment using chemoinformatics: examples from the IARC monographs on pesticides. *Environmental health perspectives*, *124*(12), 1823-1829.
3. Barupal, Dinesh Kumar, and Oliver Fiehn. "Generating the blood exposome database using a comprehensive text mining and database fusion approach." *Environmental health perspectives* 127.9 (2019): 097008.

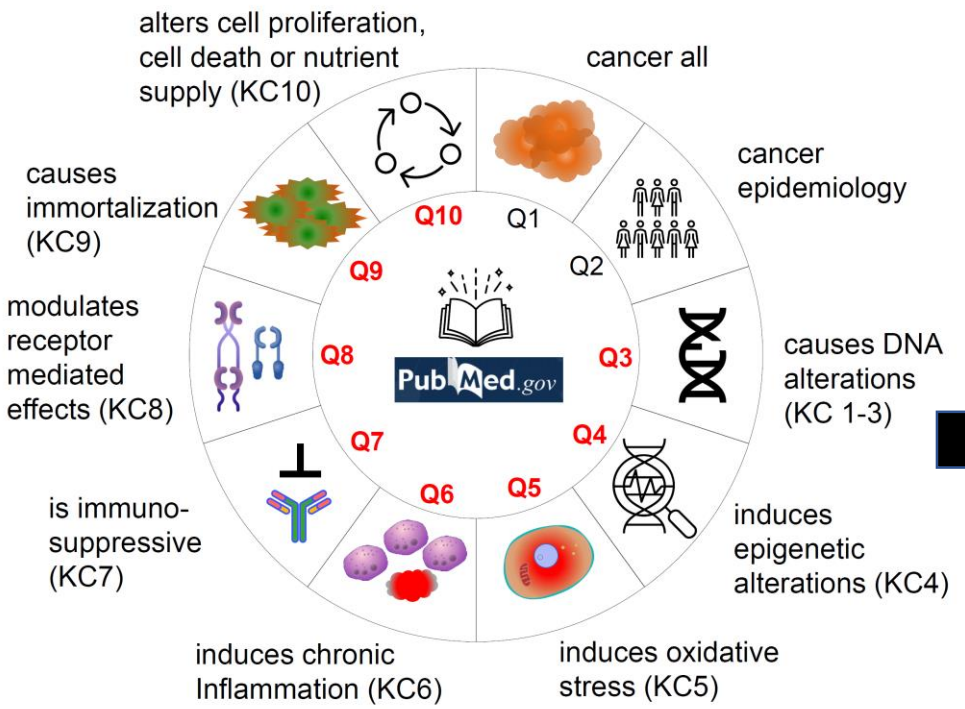
1) Chemical text mining

www.cancer.idsl.me

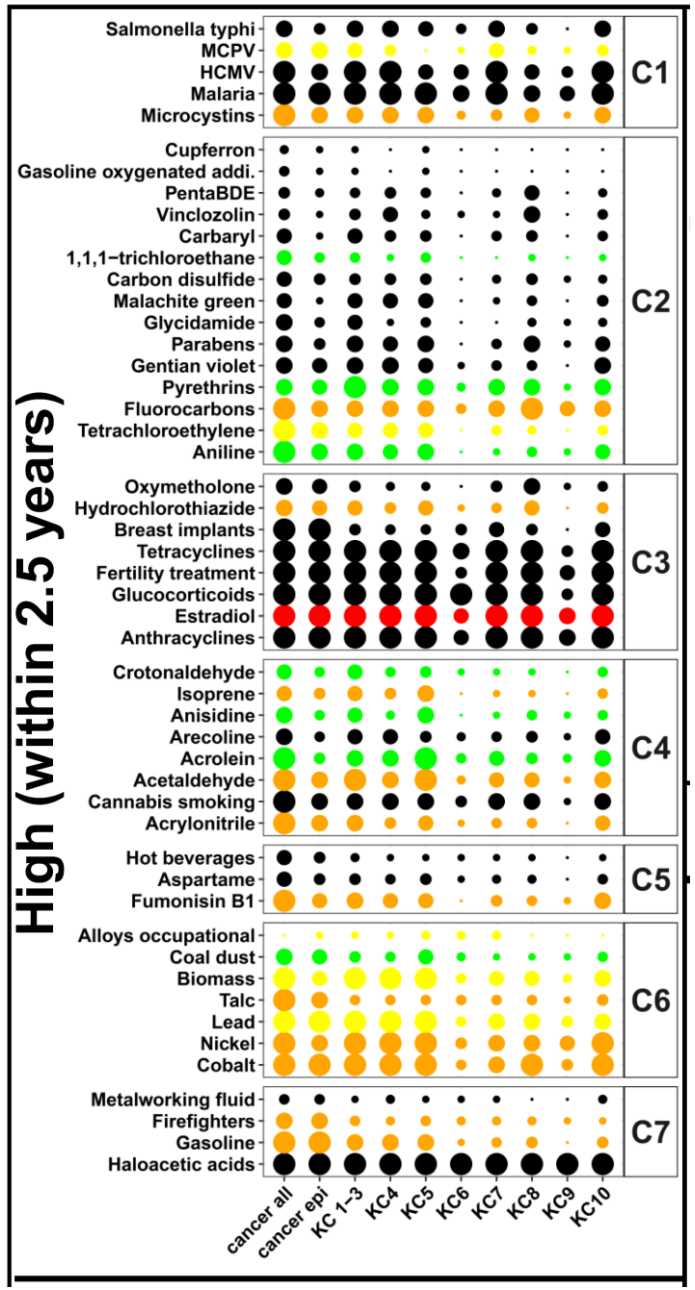
33 million abstracts

Queries

Apache Lucene Index for full-text searches



PubMed filters for key characteristics of a carcinogen (KCs)

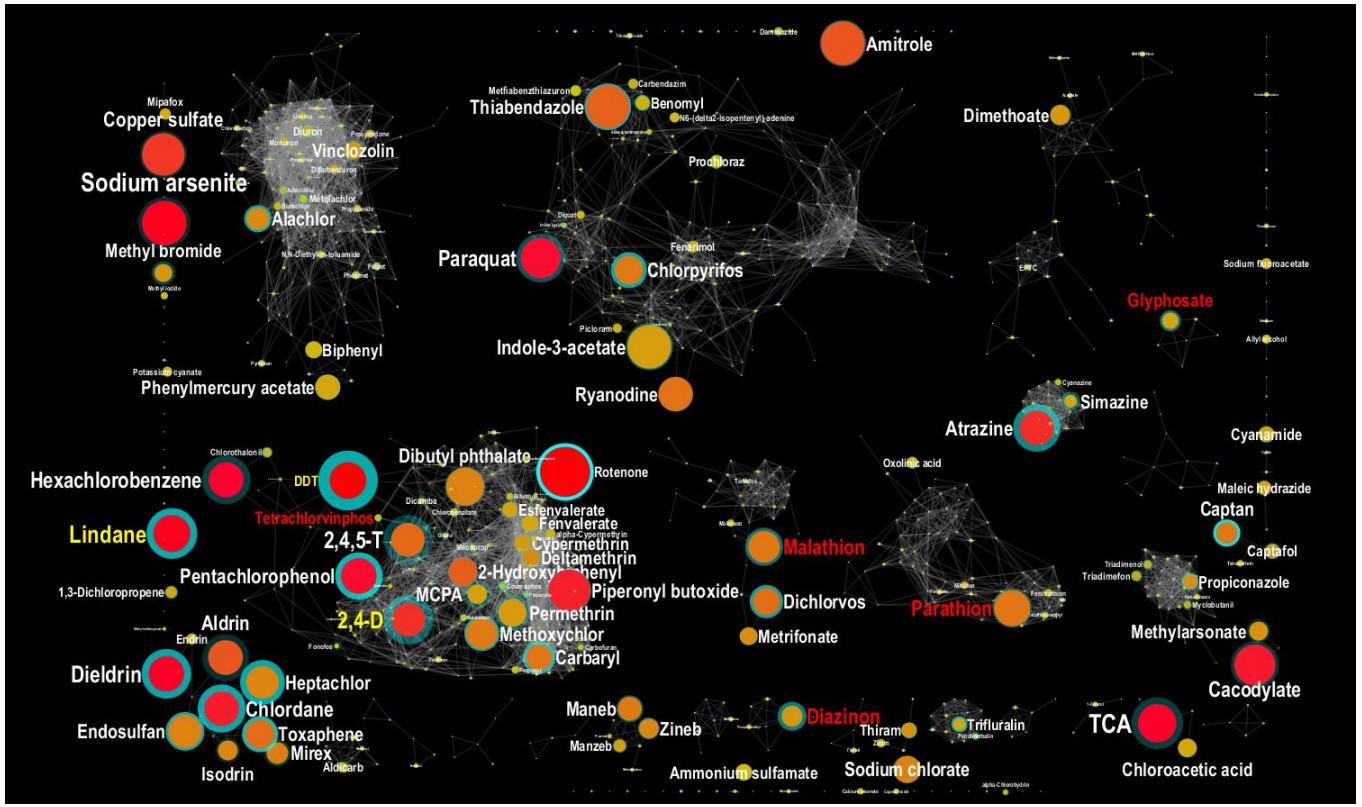


Literature count data

Provided an overview of available relevant literature data as well as highlighted the research gaps.

PMID:33984576

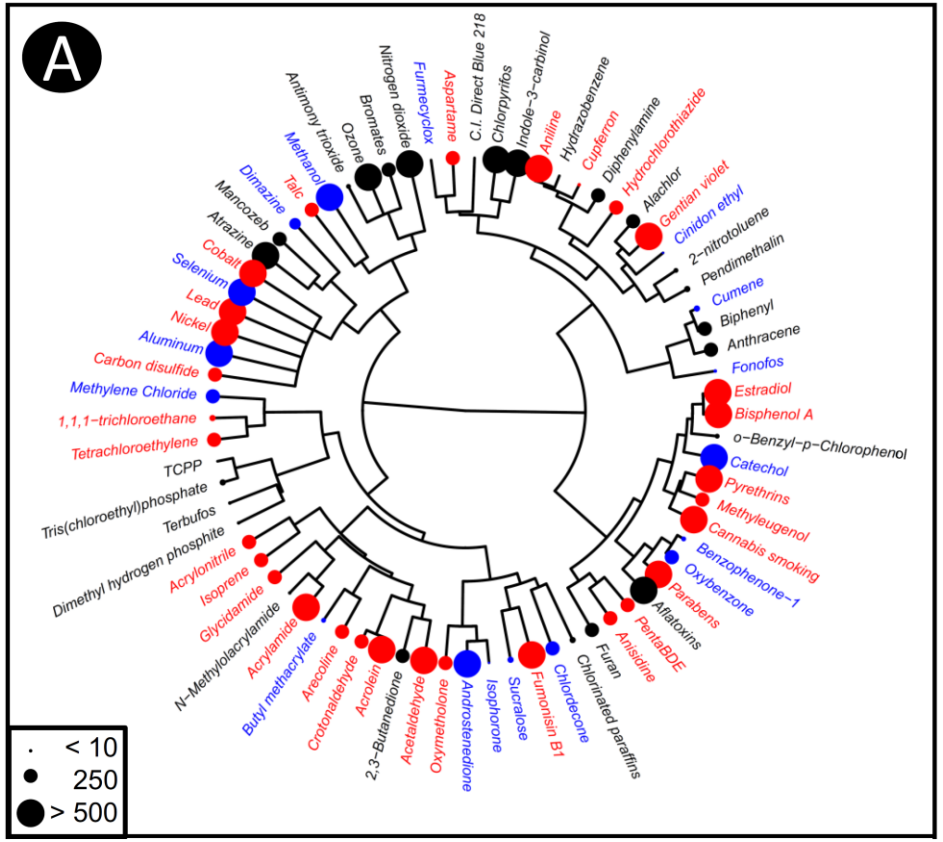
2) Chemoinformatics clustering of chemicals



Tanimoto chemical similarity coefficient

http://pesticide.barupal.org/

Chemical similarity map of ~1000 pesticides



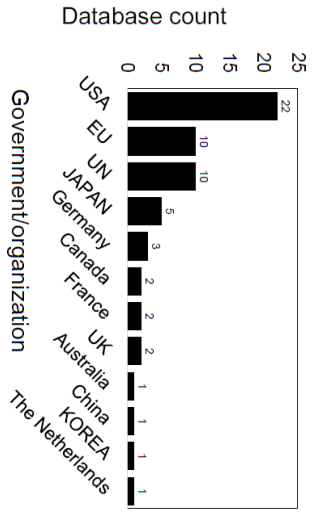
Chemical structure clustering of prioritized agents by the advisory group (2019) for IARC Monographs

Provided a logical grouping of chemically similar agents to be evaluated in a single IMO meeting.

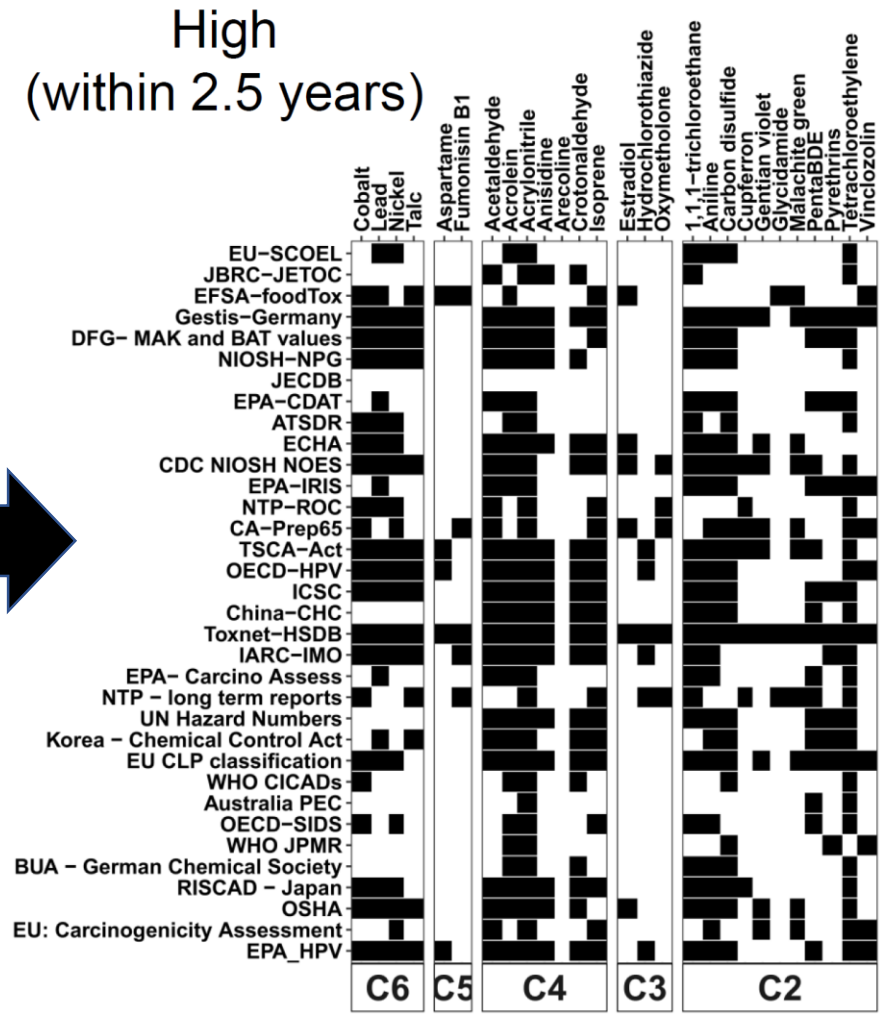
PMIDs: 33984576, 31005580, 27164621, 32593317

www.cancer.idsl.me

3) Database fusion



Database property			Database coverage				
Database	Database size	IMO coverage	All agents	High (2.5 years)	High (5 years)	Medium	Low
IARC-IMO	852	852	33	16	2	9	6
Toxnet-HSDB	5893	662	68	26	3	23	16
TSCA-Act	67270	489	52	20	3	17	12
Gestis-Germany	8014	479	62	20	3	22	17
CDC NIOSH NOES	9318	458	52	19	3	19	11
CA-Prep65	776	407	39	15	3	12	9
ICSC	1704	326	48	16	2	18	12
DFG- MAK and BAT values	1411	323	41	15	3	14	9
EU CLP classification	4007	300	50	18	3	15	14
NTP - long term reports	544	279	34	13	3	13	5
ECHA	14983	271	44	15	3	14	12
UN Hazard Numbers	2381	271	36	12	1	13	10
OECD-HPV	4636	247	43	17	2	16	8
RISCAD - Japan	4482	247	37	14	3	11	9
OSHA	901	247	40	16	2	13	9
China-CHC	2844	246	32	11	1	10	10
EPA_HPV	4308	246	43	18	2	15	8
EPA-CDAT	2626	238	31	10	2	11	8
NTP-ROC	227	198	19	9	2	4	4
EPA-IRIS	555	193	34	11	2	12	9
NIOSH-NPG	648	187	31	13	1	7	10
Korea - Chemical Control Act	2106	187	25	12	2	7	4
EU: Carcinogenicity Assessment	1243	186	24	9	1	7	7
EFSA-foodTox	5501	179	31	11	3	11	6
OECD-SIDS	1569	137	25	9	2	8	6
EPA- Carcino Assess	253	124	19	8	1	4	6
ATSDR	275	111	14	8	0	2	4
BUA - German Chemical Society	358	103	15	7	2	4	2
JBRC-JETOC	412	98	17	6	2	5	4
EU-SCOEL	269	81	14	8	2	2	2
WHO JPMR	325	60	14	5	0	8	1
WHO CICADs	346	49	9	6	0	2	1
Australia PEC	114	19	6	3	1	2	0
JECDB	445	16	1	0	0	0	1



~85,000 chemicals from 34 high priority databases

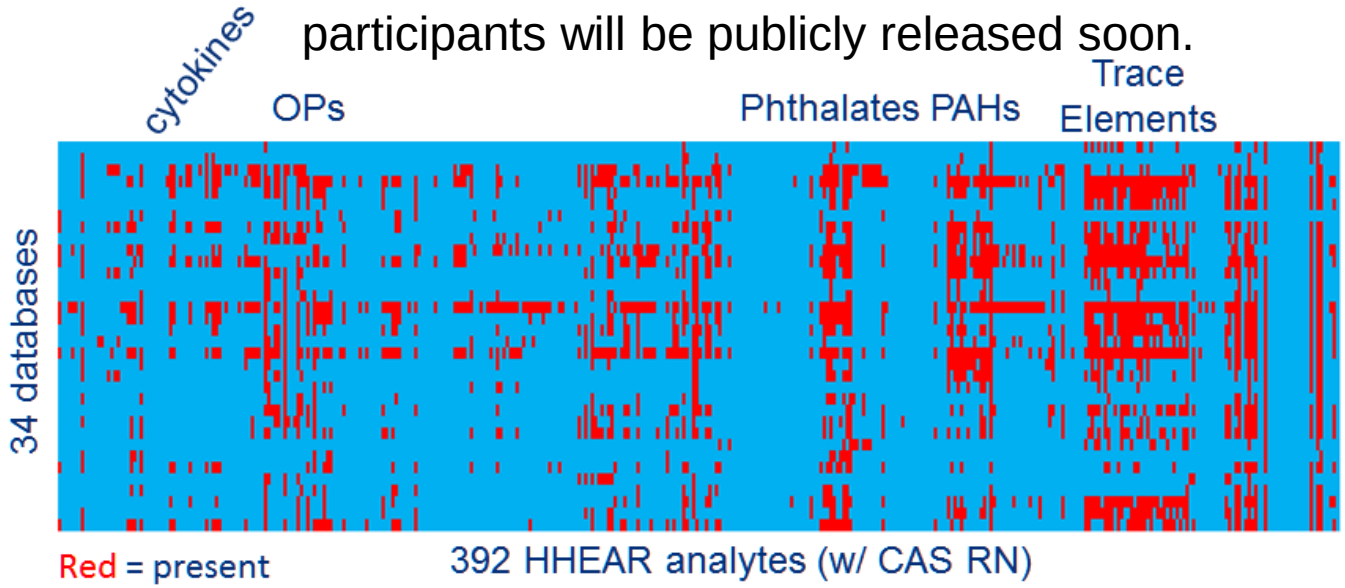
PMID: 33984576

Provided a useful list of candidate exposome chemicals and their coverage in high priority regulatory and toxicology databases.

https://chemcor.idsl.site/exposomechemicals/

Exposome and the cancer hazard identification

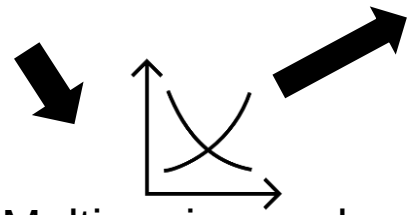
Data from 40 studies and ~28,000 participants will be publicly released soon.



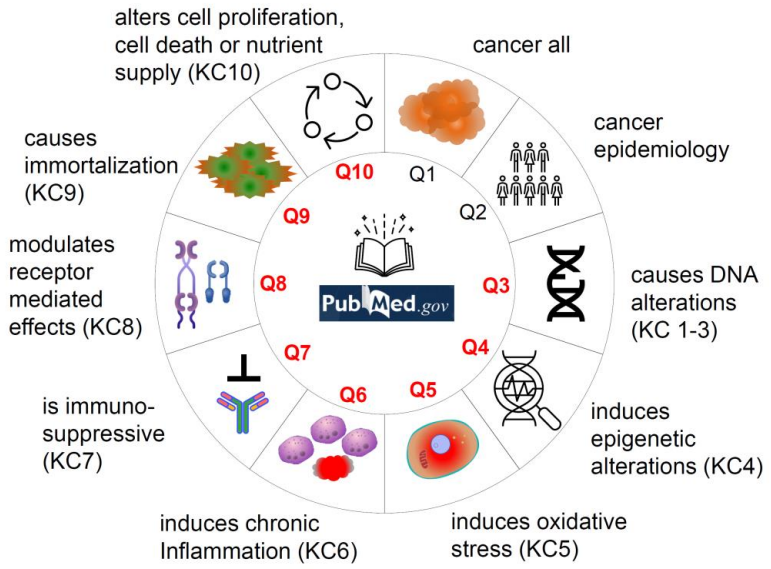
Liquid or gas chromatography
+ high resolution mass spectrometry
+ ipa.idsl.me

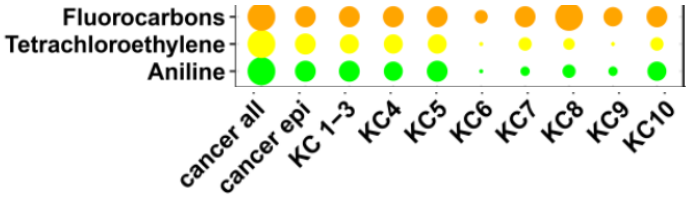
> 50,000 unique chemicals

Biomonitoring surveys using targeted and untargeted chemical analysis assays



Multi-omics analyses





HHEAR Human Health Exposure Analysis Resource

https://hhearprogram.org/

Exposome research have a great potential to fill gaps in the evidence-base for cancer hazard identification. HHEAR public data will be a first of its kind to support such investigations.

Conclusions

1. IARC Monographs uses a systematic and complex process to identify cancer hazards.
2. The process requires engagement among public, scientific experts, advisory board and IMO scientists.
3. The process can be benefitted by a data science approach of chemical text mining, chemoinformatics and database fusion to prioritize agents.
4. A computational approach has been developed to facilitate agent prioritization (cancer.idsl.me).
5. Exposome research has a great potential to fill research gaps in key characteristics of an agent to be classified as a carcinogen.

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HHEAR Human Health Exposure Analysis Resource