NTP
National Toxicology Program

Environmental Influences on the Epigenome: Using SWIFT Text Mining Tool to Explore the State of the Science

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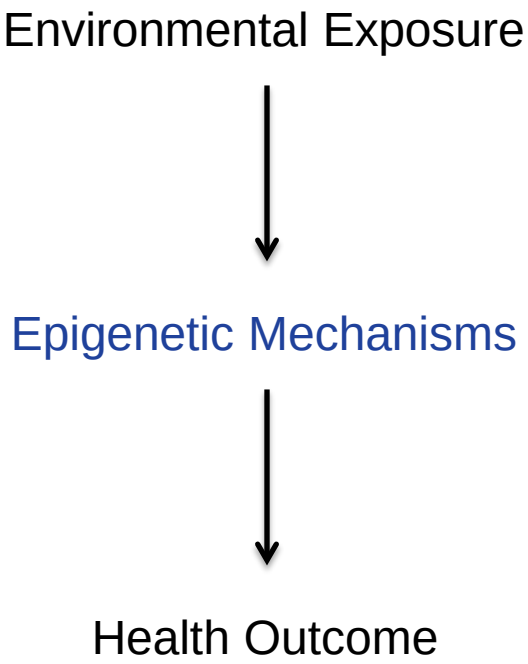
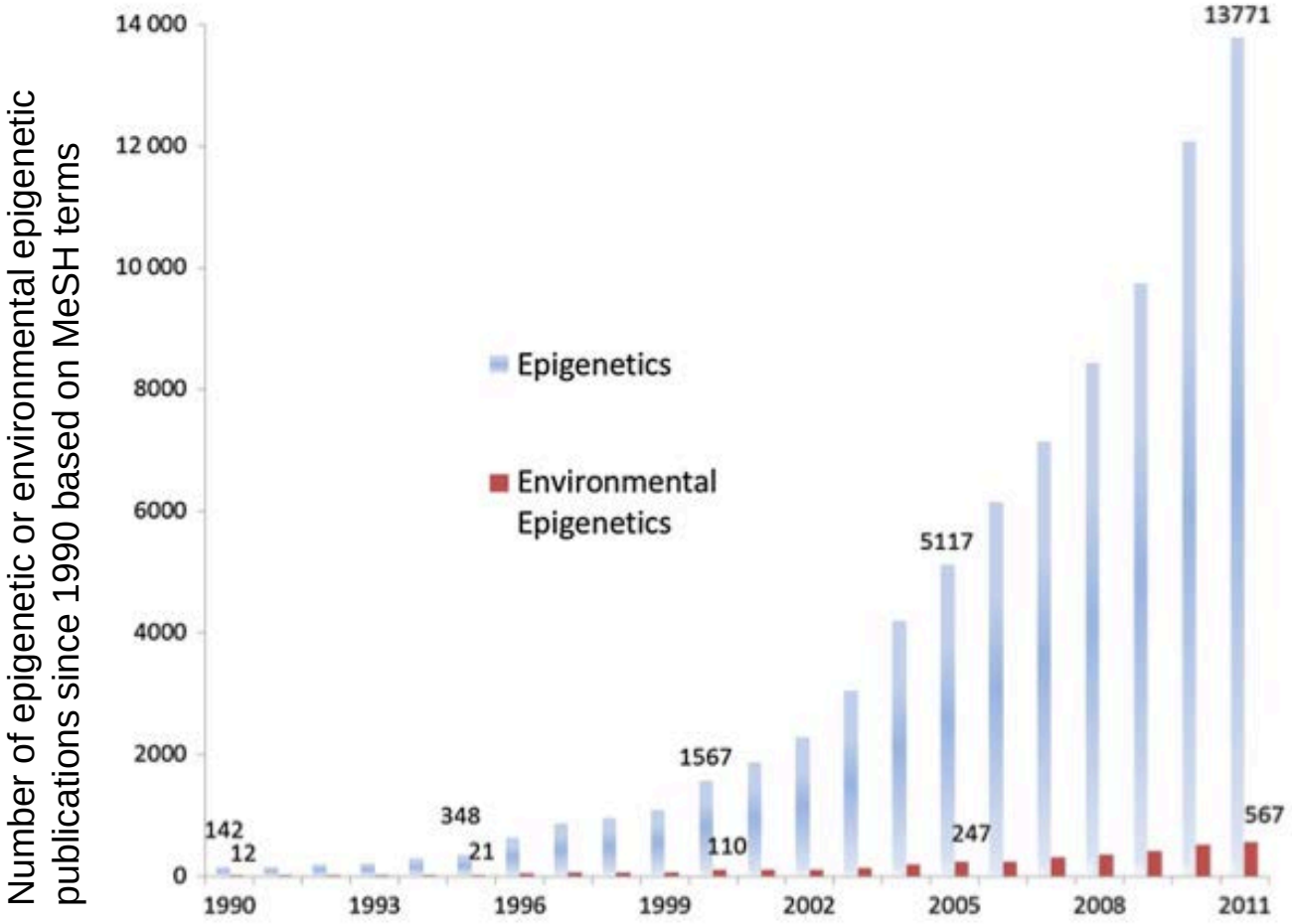
NTP Board of Scientific Counselors Meeting
June 16, 2015

Where are these links the strongest?



There is a growing interest in epigenetics

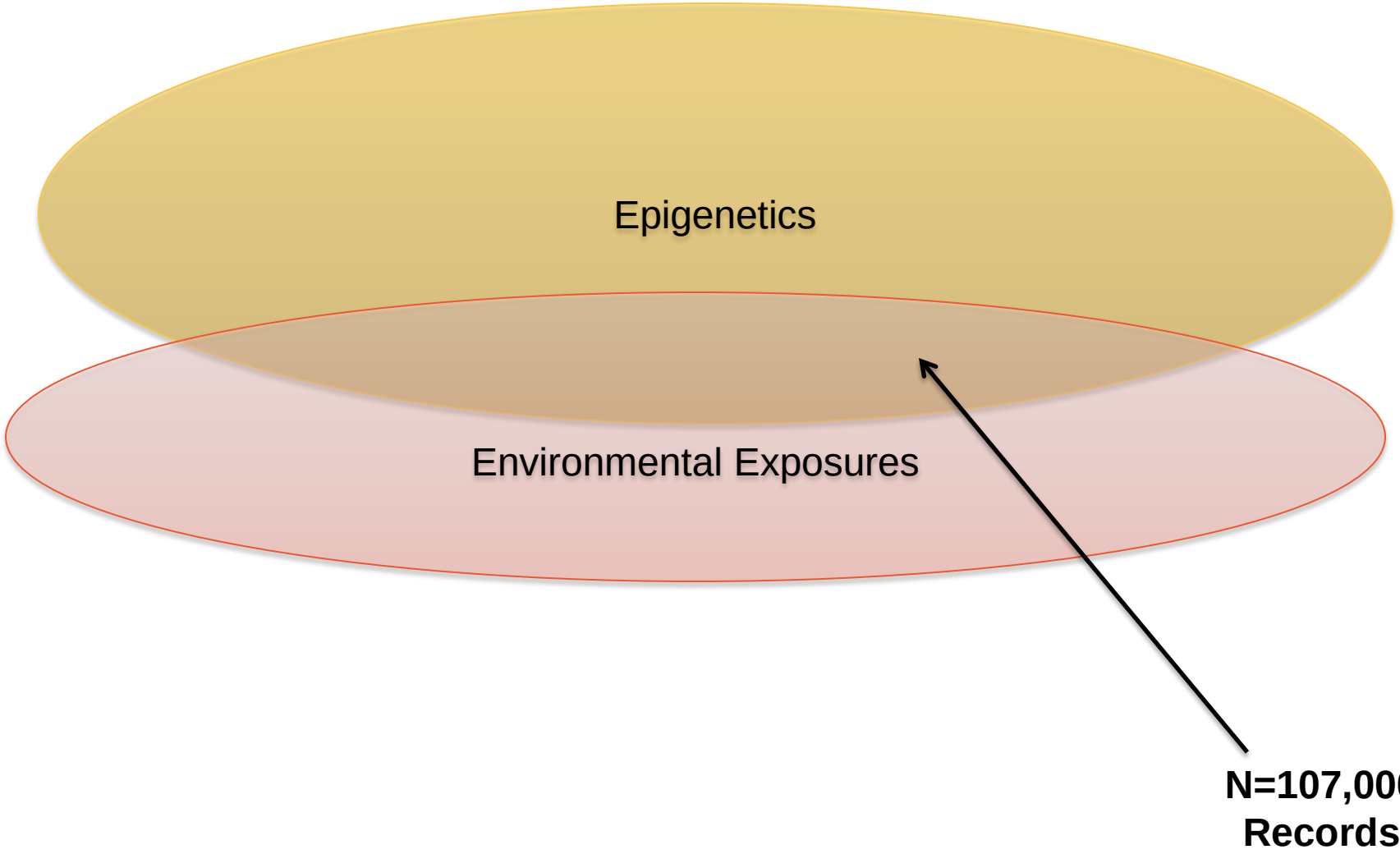


Burris HH, Baccarelli AA. 2014. Environmental epigenetics: From novelty to scientific discipline. J Appl Toxicol 34:113-116.

Addressing the need

- 2012-2017 NIEHS Strategic Plan
  - "*the effects of the environment on the epigenetic regulation of biological and pathological processes*"
- Cross-divisional implementation group
  - *"Where are the links between environmental exposures and health outcomes via epigenetic mechanisms the strongest?"*
- Evaluation design team

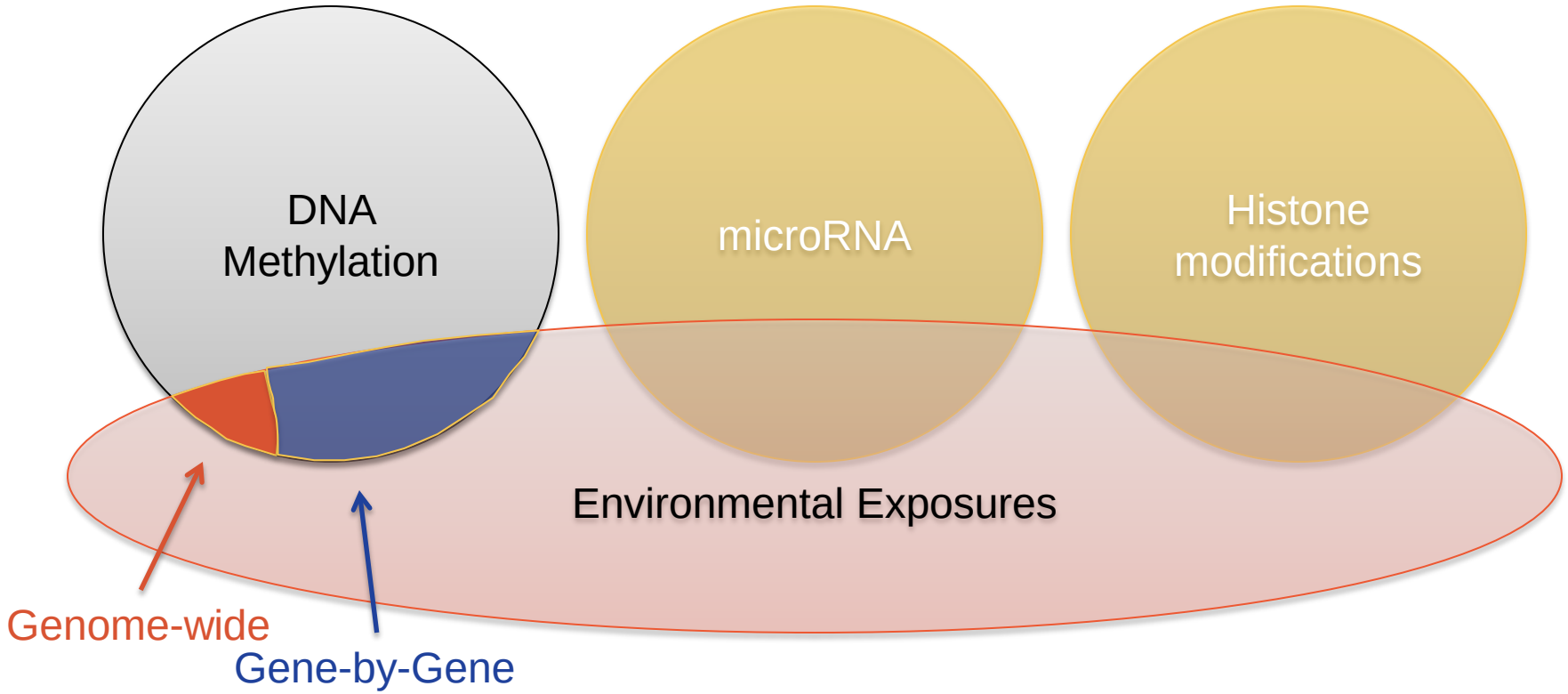
How was the research question refined?



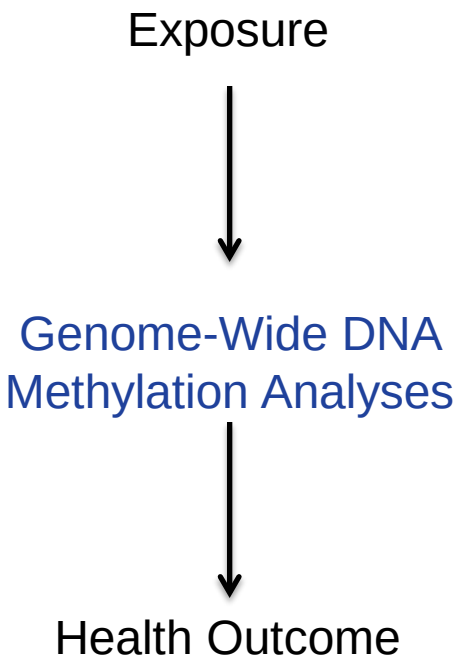
How was the research question refined?

- More focused research question
- Test drive text-mining and machine learning tools
- Develop a new report format (“scoping report”)

How was the research question refined?



What is the extent of the evidence?



Specific Aims

- Search for genome-wide analyses of DNA methylation
- Identify literature for seed sets
- Relevancy rank the search results
- Categorize records by type of exposure, health outcome, and evidence stream (human, animal, *in vitro*)
- Visualize the results

SCOPING REPORT

How was the literature search crafted?

- Global DNA methylation
- DNA m
- Genon
- Genon
- Epiger

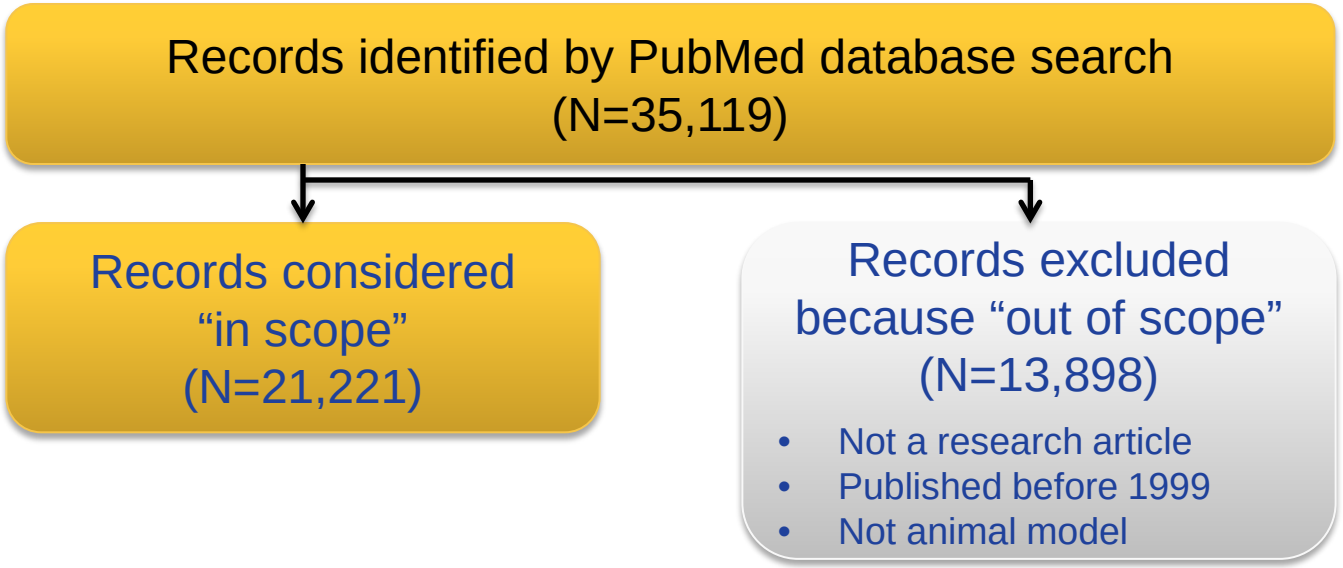
DNA METHYLATION - Search "DNA Methylation"[mh] OR ((DNA[mh] OR DNA[tiab] OR cytosine[mh] OR cystosine*[tiab] OR Alu[tiab] OR LINE-1[tiab] OR genes[tiab] OR genom*[tiab]) AND methylat*[tiab]) OR "CpG islands"[mh] OR ((CpG[tiab] OR CpGs[tiab] OR CPG's[tiab] OR non-CG[tiab] OR non-CPG) AND methylat*[tiab]) OR differential-methylat*[tiab] OR differentially-methylated[tiab] OR partially-methylated[tiab] OR "partial methylation"[tiab] OR hemimethylat*[tiab] OR hemi-methylat*[tiab] OR hypermethylat*[tiab] OR hyper-methylat*[tiab] OR hypomethylat*[tiab] OR hypo-methylat*[tiab] OR demethylat*[tiab] OR unmethylat*[tiab] OR nonmethylat*[tiab] OR DNA modification methylases[mh] OR methylas*[tiab] OR demethylas*[tiab] OR methyltransferase*[tiab] OR "DNA Mtase"[tiab] OR Dnmt*[tiab] OR 5-methylcytosine[mh] OR "5-methylcytosine"[tiab] OR 5-methyl-cytosine[tiab] OR 5mc[tiab] OR 5meC[tiab] OR Hydroxymethylat*[tiab] OR 5-hydroxymethylcytosine[tiab] OR 5-hydroxy-methylcytosine[tiab] OR 5-hydroxymethyl-cytosine[tiab] OR 5hmC[tiab] OR Methyl-binding-domain*[tiab] OR methyl-binding-protein*[tiab] OR MBD2*[tiab] OR MBD3*[tiab] OR MBD4*[tiab] OR "methyl-cpg-binding protein 2"[mh] OR methyl-CpG*[tiab] OR MeCP2[tiab]

Global DNA methylation OR

(Epigenetics OR DNA methylation) AND
(genome-wide OR genome-wide techniques)

N=35,119 records retrieved

How were records processed?

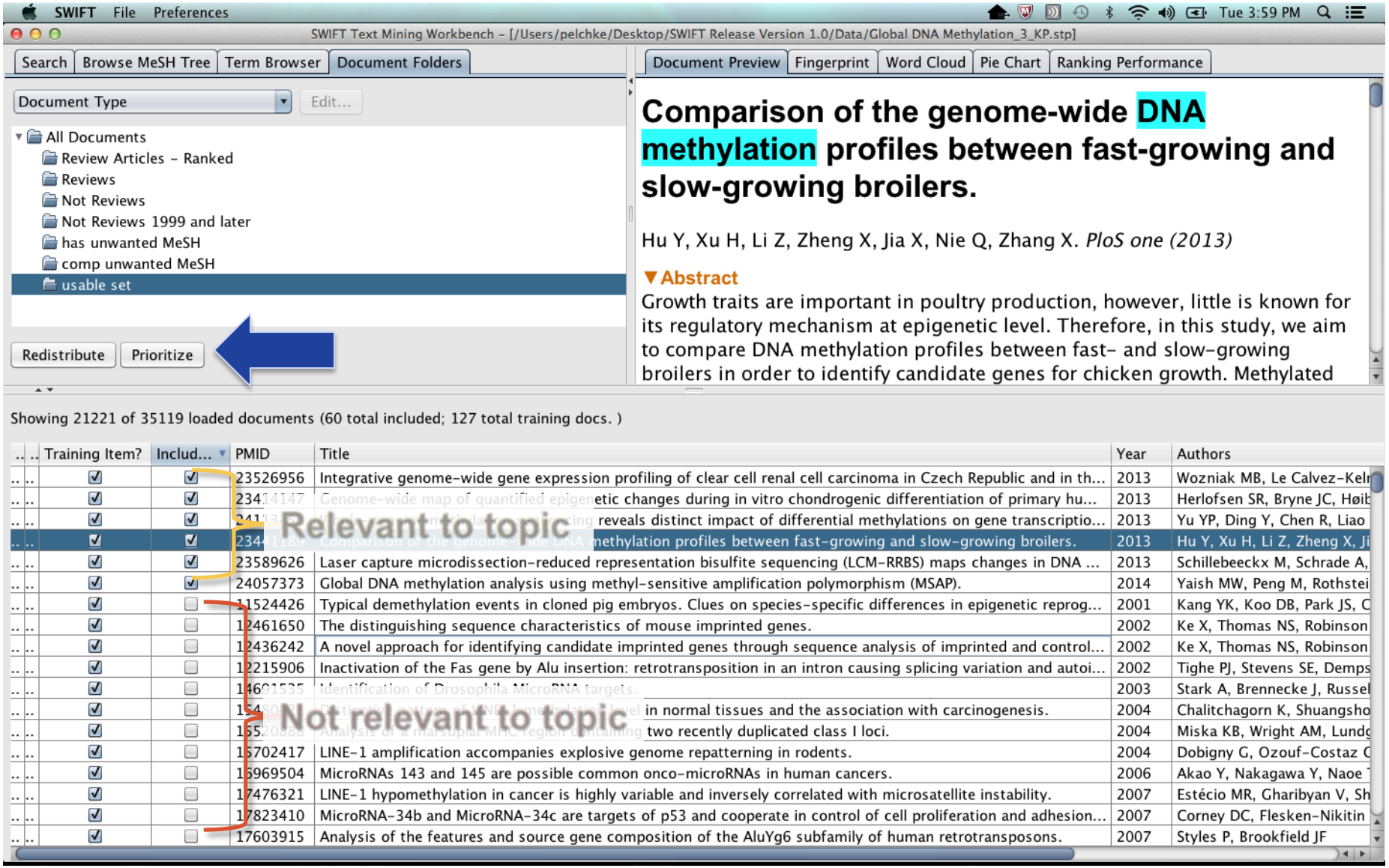


What topics are in this literature?

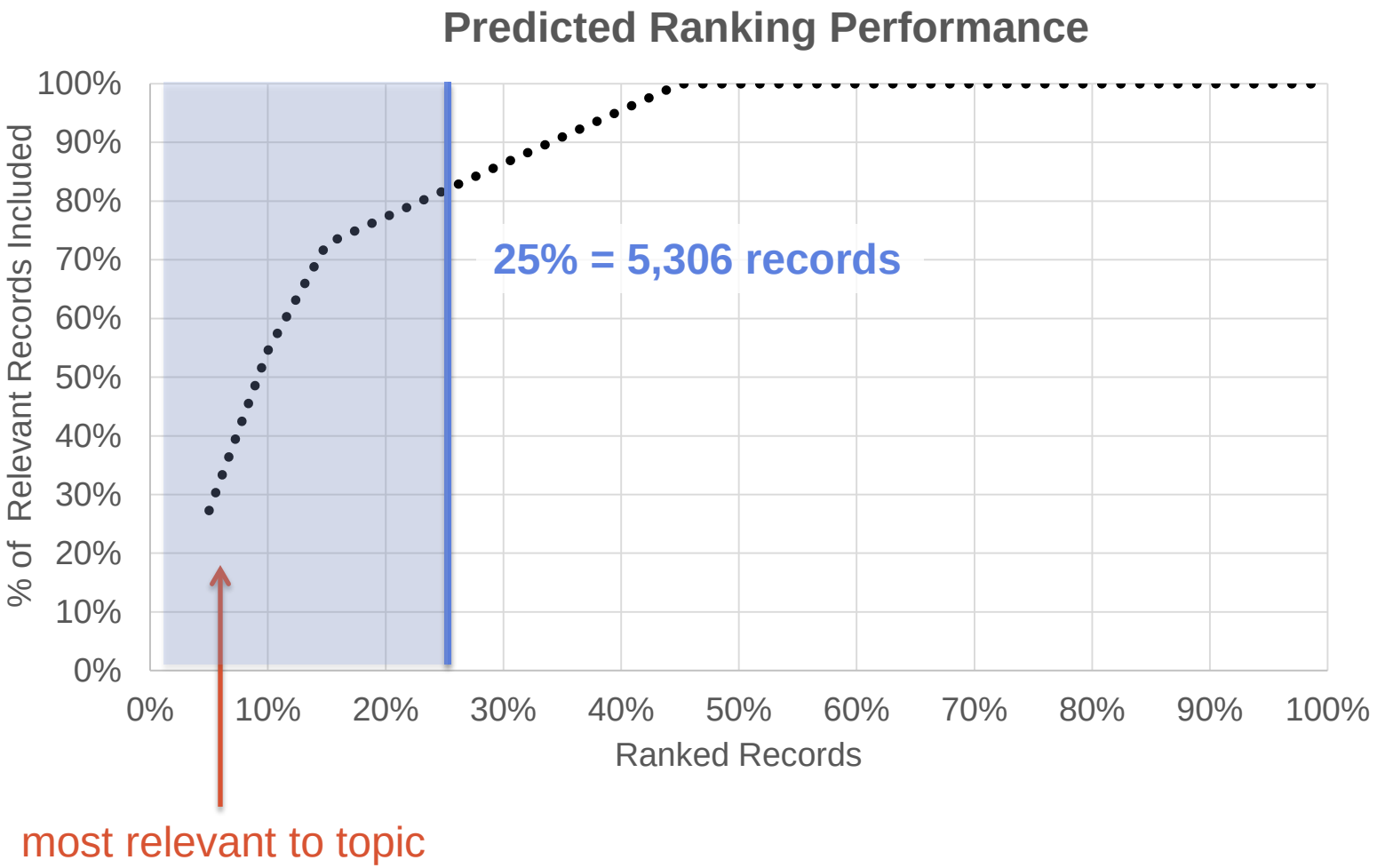
	# records
Topic 28: genes, expression, gene, analysis, identified, microarray, expressed, involved, identify, genome-wide	11778
Topic 41: epigenetic, mechanisms, development, gene, genetic, studies, disease, epigenetics, regulation, recent	8637
Topic 40: methylation, dna, cpg, methylated, promoter, island, sites, islands, human, regions	7869
Topic 29: cell, cells, growth, signaling, expression, kinase, apoptosis, protein, proliferation, pathway	6793
Topic 11: transcription, promoter, gene, binding, expression, transcriptional, factor, sites, regulation, region	6208
Topic 2: histone, chromatin, epigenetic, modifications, acetylation, gene, modification, methylation, dna, lysine	4933
Topic 21: cancer, prostate, expression, cell, cells, tumor, pancreatic, human, lines, invasion	3491
Topic 38: histone, protein, proteins, complex, domain, mbd, polycomb, ezh, binding, silencing	3392
Topic 48: protein, proteins, mitochondrial, stress, cells, cellular, nuclear, membrane, cell, oxidative	3259

- 50 topics are automatically generated based on the most frequently used words
- Topics were surveyed to get a sense of the types of records that had been retrieved
- Topics were screened and ~120 records were identified to serve as a seed set (60 relevant ★ 67 not relevant ✖)

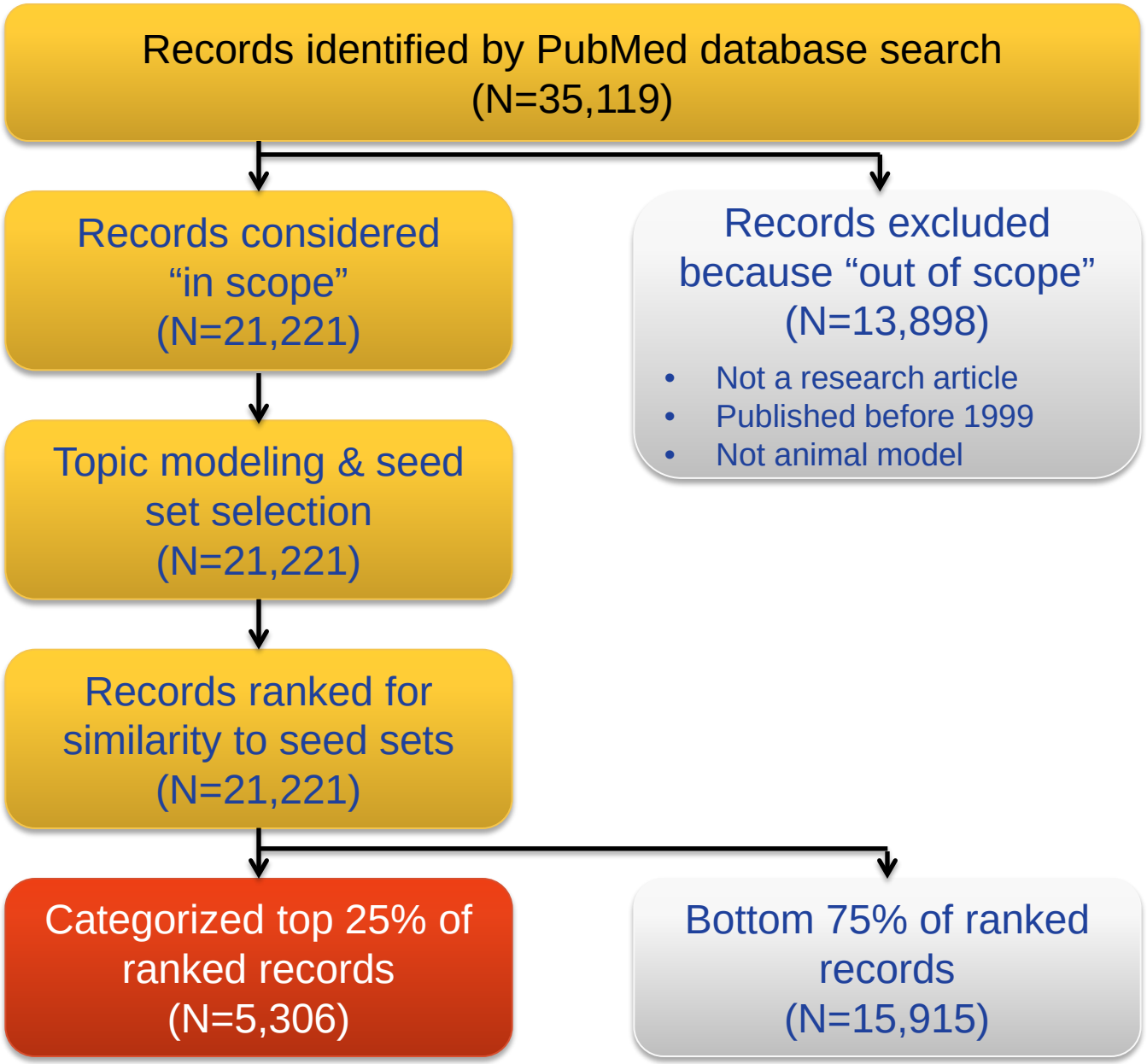
How do the records compare to seed sets?



Which were the most relevant records?



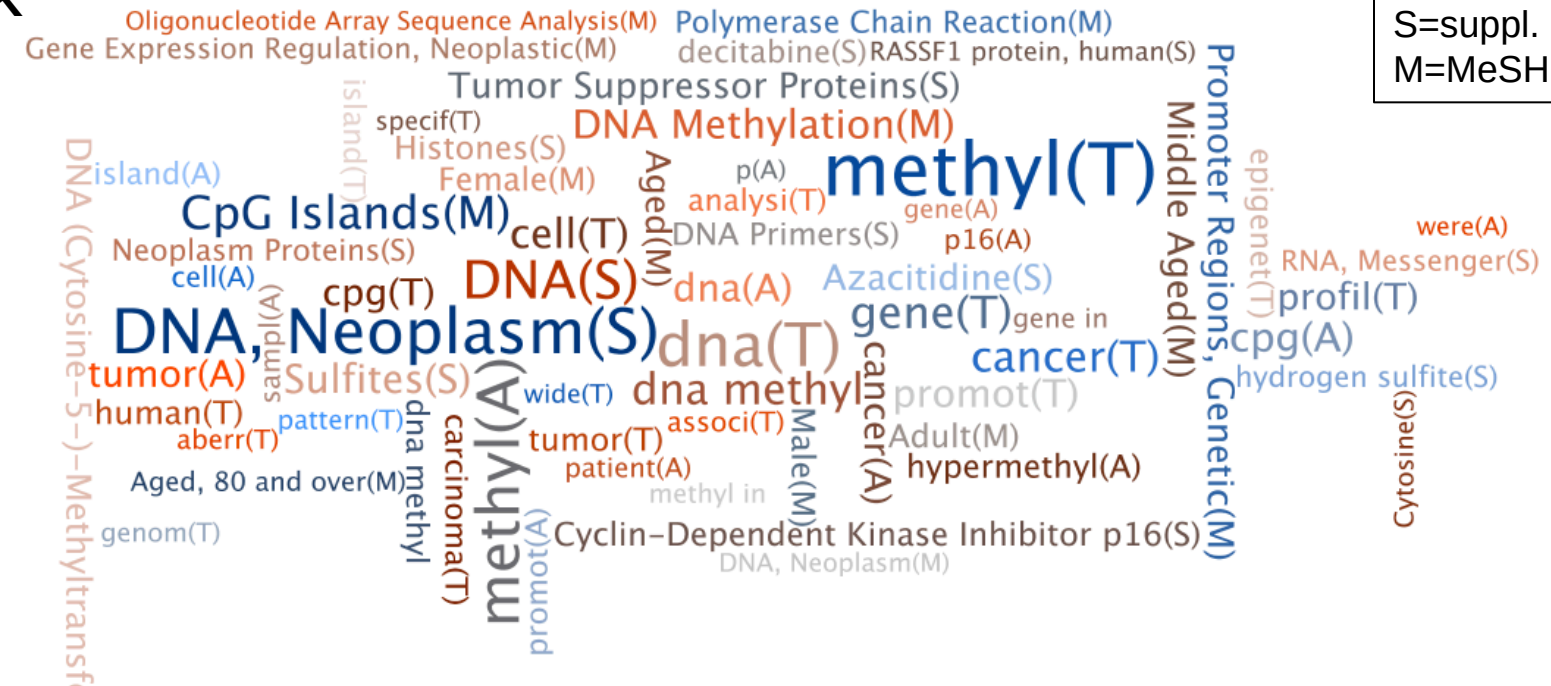
How were records processed?



How effective was the enrichment?

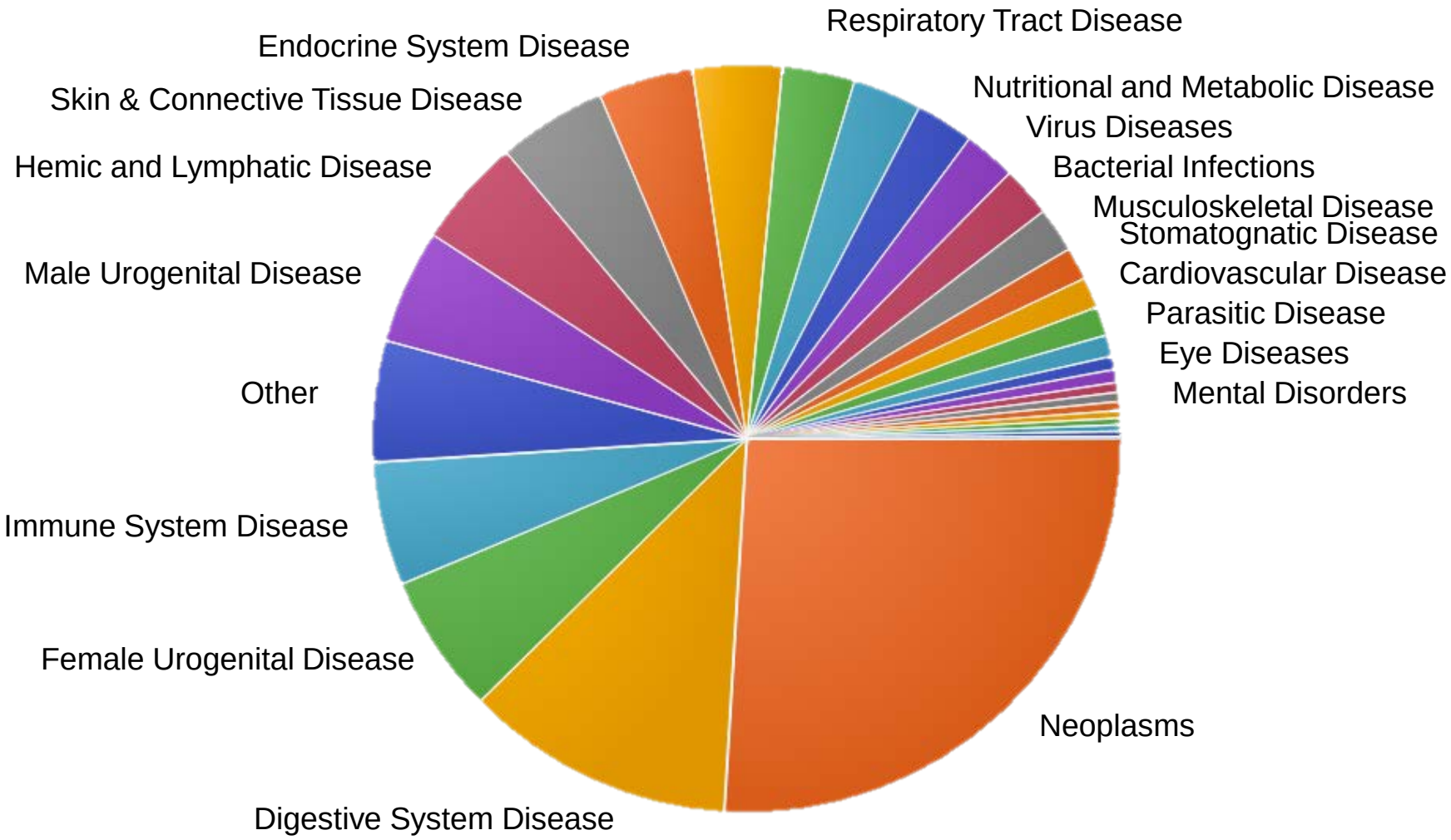
Original
N=35K

Top 25%
N=5K



T=title
A=abstract
S=suppl. info
M=MeSH

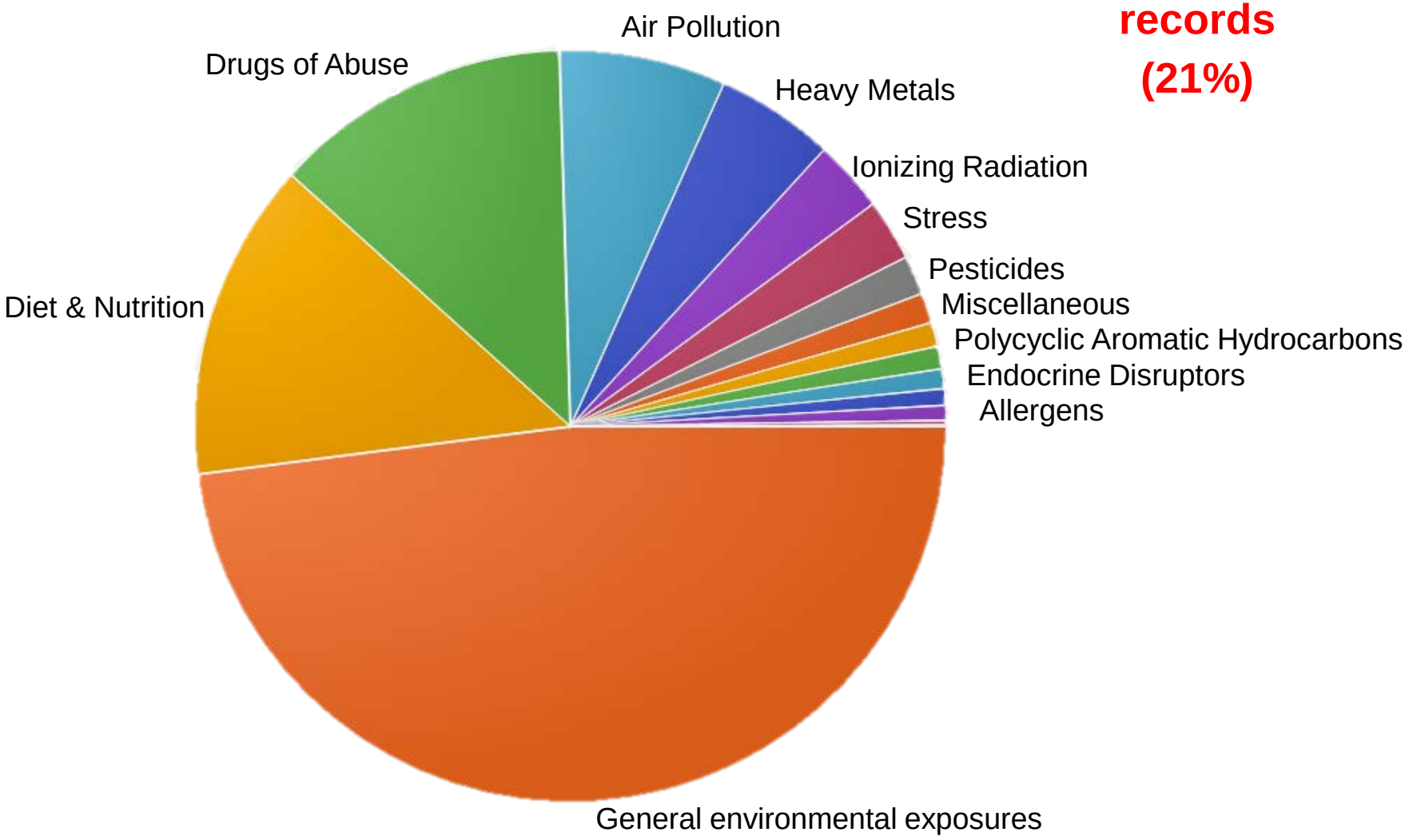
What health outcomes are investigated?



N=5,306 records

What types of exposures are investigated?

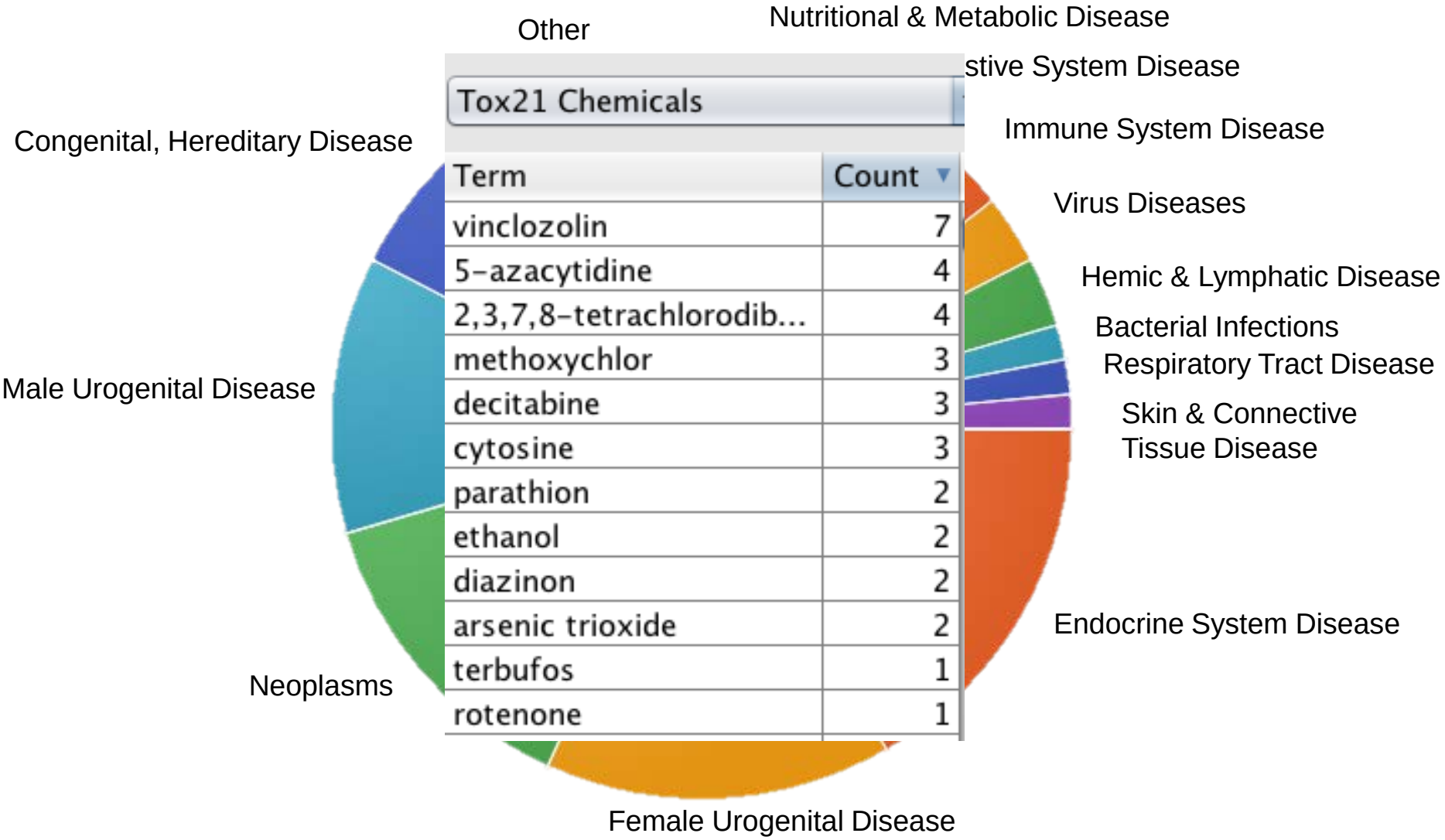
N=1,130 of 5,306 records (21%)



Evaluating exposure & health outcomes

Exposure = pesticide

N=26 records



Term	Count
vinclozolin	7
5-azacytidine	4
2,3,7,8-tetrachlorodib...	4
methoxychlor	3
decitabine	3
cytosine	3
parathion	2
ethanol	2
diazinon	2
arsenic trioxide	2
terbufos	1
rotenone	1

Summary

- Scoping reports useful for large, complex or emerging literatures
  - Get a sense of the literature
  - Highlights the variety in the field
  - Line up future projects
  - Research tool for data mining
- Implemented a new text mining tool
  - Useful for visualizing

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