What We Know and What We Don't: Investigating the Carcinogenic Potential and Gene Expression Patterns of Plastic Additives

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Introduction

- Plastic additives are chemical compounds that expand the utility of plastics, but they have the potential to contaminate soil, air, water, and food and contribute negatively to our health.[1]
- A typical American consumes and inhales up to **121,000 microplastics** per year, and bottled water consumption further increases this number. [2]
- Plastic particulate has been detected in human tissue samples such as the lungs, colon, and placentas. [3, 4, 5]
- There is an urgent need to determine the health impacts of the plastic additive mixtures that are incorporated and processed with raw polymers.

Research Goals and Methods

1.

Complete literature review to compile list of high-confidence plastic additives (intentionally or unintentionally added).

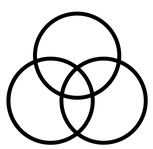
2.

Query additive list in three cancer & toxicology databases (IARC, IRIS, and EcoTox) to determine extent of knowledge on additive carcinogenicity.

3.

Extract gene expression data associated with each additive from the Comparative Toxicogenomics Database (CTD) and determine enriched pathways using WebGestalt.

4.



Compare gene expression profiles of known carcinogenic additives to additives with uninvestigated or unclear carcinogenicity.

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Results

Many plastic additives are carcinogens, but 90% have unknown cancer-causing potential.

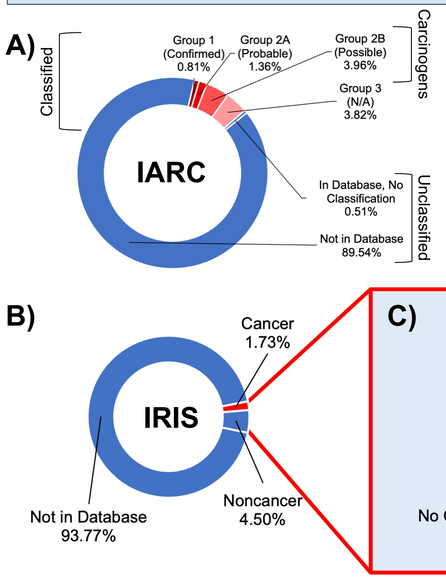

Figure 1: The majority of plastic additives from the literature review are not documented in the IARC or IRIS databases. A) Approximately 90% of the 2,712 plastic additives have no cancer classification in the WHO IARC database (1: Carcinogenic, 2A: Probably carcinogenic, 2B: Possibly carcinogenic, 3: Not classifiable as to its carcinogenicity to humans). **B)** Almost 94% of the additives are not in the EPA IRIS database. **C)** Further classifications of the Figure 1B 'cancer' categories in the IRIS database.

Most additives lack public descriptions of their functions, end products, and gene expression effects.

The top polymers and product types are each linked with hundreds of additives, raising concerns about chemical cocktails in everyday plastics.

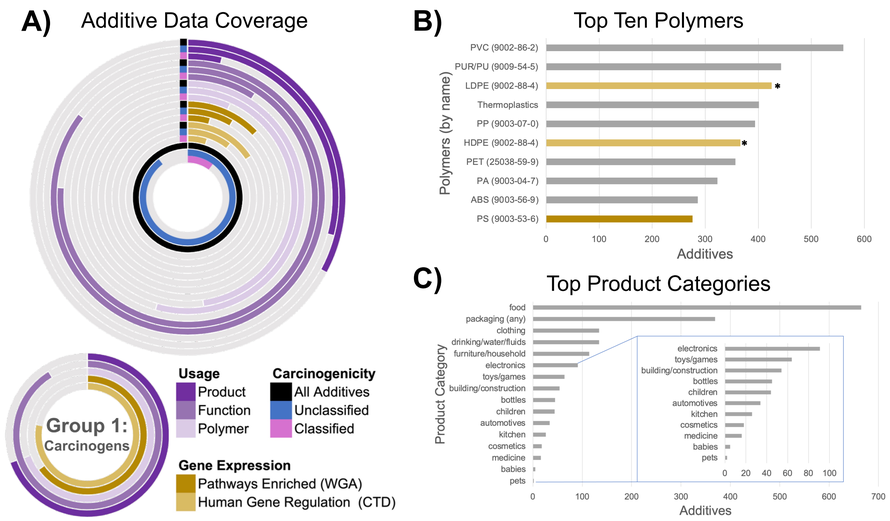

Figure 2: Plastic additives overwhelmingly lack basic descriptive data, gene expression data, and cancer classifications. A) 85% of additives are associated with functional data, 55% are linked to the polymers that incorporate them, 33% are mappable to consumer products, and 13% are associated with sufficient gene expression data to complete pathway enrichment analysis. Group 1 carcinogens are significantly better studied with regards to gene expression than Groups 2A, 2B, 3, or unclassified. **B-C)** Polymers and product categories with the most additive associations. **B**) **LDPE and HDPE share the same CAS number.* CTD included gene expression data describing LDPE/HDPE and PS. Only PS was viable for WebGestalt's Over-Representation Analysis. **C)** Food, packaging, clothing, and drinking-related products use the most additives.

Carcinogenic and unclassified additives cluster together based on biological pathway enrichment.

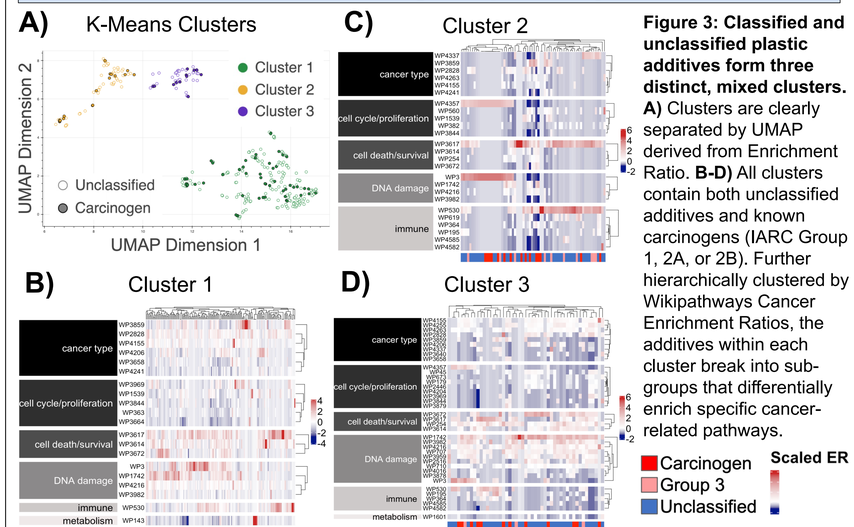

Figure 3: Classified and unclassified plastic additives form three distinct, mixed clusters. A) Clusters are clearly separated by UMAP derived from Enrichment Ratio. **B-D)** All clusters contain both unclassified additives and known carcinogens (IARC Group 1, 2A, or 2B). Further hierarchically clustered by Wikipathways Cancer Enrichment Ratios, the additives within each cluster break into sub-groups that differentially enrich specific cancer-related pathways.

Additive clusters are associated with cancer, immune response, and liver pathways.

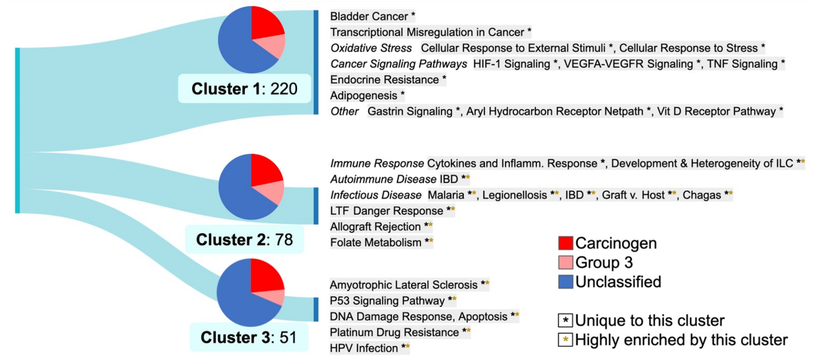

Figure 4: Characterization of full dataset after Over-Representation Analysis (349 additives) and further breakdown across three major clusters by their associated pathway enrichment.

Conclusions

1. Over 150 additives have known carcinogenic potential.
2. **There is a significant gap in current knowledge regarding the carcinogenicity of plastic additives.** The similar gene expression profiles of classified and unclassified additives underscore the need to test thousands more additives for carcinogenic behavior.
3. Gene expression pathways impacted by plastic additives are related to DNA damage, apoptosis, immune response, viral diseases, and cancer.

References & Acknowledgements

References:

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