Integration of Gene Expression Data and Glyphosate Toxicity: Overlap Between Murine Models and the Comparative Toxicogenomics Database

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INTRODUCTION: Glyphosate-based herbicides are the most used pesticides in crops around the world, since its registration in 1974. The Environmental Protection Agency (EPA) classifies this pesticide as “not likely to be carcinogenic to humans”, disagreeing with the International Agency for Research on Cancer (IARC). Thus, glyphosate safety is a controversial issue among the scientific and governmental community. OBJECTIVE: In order to evaluate the toxicity of glyphosate and potential risks for human and animal health This study aimed to characterize, at the molecular level, the effects of glyphosate in murine models by integrating curated chemical-gene interaction data (CTD) with gene expression profiles from mice exposed to herbicide, to identify priority biological targets in experimental toxicology. METHODS: Gene expression data from *Mus musculus* exposed to glyphosate were obtained from the GEO database (dataset GSE253299). Differential expression analysis was performed using the *limma* package, with genes considered significant at |log2FC| > 1 and adjusted p-value < 0.05 (Benjamini-Hochberg correction). Glyphosate-associated genes were retrieved from the Comparative Toxicogenomics Database (CTD), filtered for "glyphosate" interactions and "*Mus musculus*" species specificity. Intersection analysis between CTD-derived genes and differentially expressed genes (DEGs) from GSE253299 was conducted using the *VennDiagram* package, followed by functional enrichment analysis of overlapping genes. Enriched Gene Ontology (GO) terms (Biological Process) and KEGG pathways were identified via *clusterProfiler*, with significance thresholds set at false discovery rate (FDR) < 0.05 and a gene count ≥ 5 per term. Redundant GO terms were simplified using semantic similarity analysis (cutoff = 0.7). RESULTS AND CONCLUSION: The intersection between DEGs and CTD data presented 218 genes. The functional enriched pathways include: “Breast Cancer”, “MicroRNAs in Cancer”, “PI3K-Akt Signaling Pathway”; while GO terms enrichment included Biological Processes such as “Cellular response to abiotic stimulus”, “cellular response to environmental stimulus” and “response to radiation”. Our findings suggest that glyphosate exposure modulates cancer-associated pathways and stress-response mechanisms and further supports glyphosate’s role as a cellular stressor, potentially through oxidative or genotoxic mechanisms. These results highlight key molecular pathways disrupted by glyphosate in murine models and underscores the importance of experimental toxicogenomics in clarifying the health risks of widely used herbicides.