A198 · OMNIA: Structural Graph Autoencoder Mapping of Microplastic-Induced Respiratory Gene Regulation

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Micro- and nanoplastics (MNP) are a rapidly escalating global exposure burden, with airborne concentrations reaching tens of thousands of particles per day and polymer fragments detected in over 80% of examined human lung specimens. No structural, cross-cell-type regulatory map exists for how MNP rewire respiratory biology, and standard differential expression and WGCNA pipelines fail to recover reproducible signal across heterogeneous datasets.

We present the OMNIA Microplastic Regulatory Network, a reproducibility-first pipeline integrating three independent human respiratory transcriptomics datasets (nasal epithelium, bronchial epithelium, pulmonary fibroblasts; 63 samples) into a unified 9,829-gene, 408,913-edge co-expression graph. A two-layer Graph Convolutional Network autoencoder (GCN-GAE) trained on PCA-derived node features achieves high-fidelity structural encoding (Test AUC = 0.9766; AP = 0.9684; F1 = 0.9336), outperforming feature-only baselines (>0.03 AUC gain) and ablation controls while maintaining strict adjacency-leakage isolation.

PGExplainer across 2,000 nodes extracts a 25,000-edge Core Regulatory Backbone, yielding six global-hub Leiden modules (n > 100 genes, q <= 0.05) after pathway enrichment (GO, KEGG, REACTOME): ciliary IFT-B disruption (q=1.2e-11; q=1.1e-10), metabolic-stress/autophagy (q=0.036), RNA/translational overload (q=1.9e-15), genomic instability (q=0.0036), G1/S checkpoint (q=1.7e-5), and MET-FAK remodeling (q=0.021). Hub and driver genes across modules were consolidated into a 55-gene OMNIA signature, enabling LINCS L1000FWD drug-reversal analysis; naproxen and zileuton show reversal similarity <= −0.20 (Bonferroni q < 0.05), nominating them as candidate compounds for experimental validation.

OMNIA demonstrates how graph autoencoding and GNN explainability resolve reproducible cross-dataset regulatory structure, providing a scalable, generalizable framework for environmental toxicogenomics research.