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Transcriptomic profiling reveals distinct mitochondrial and metabolic pathway alterations induced by PFOA in A549 and HepG2 cells

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Perfluorooctanoic acid (PFOA) is a persistent environmental pollutant with potential toxicological effects, yet its molecular impact on cancer cells remains insufficiently characterized. In this study, we performed bulk RNA-sequencing of A549 (lung) and HepG2 (liver) cells following 24-h low-dose PFOA exposure. Principal coordinate analysis of variance-stabilized transcriptomes indicated modest but noticeable separation between control and treated groups in both cell lines.

Functional enrichment analyses revealed cell line–specific transcriptional responses. In A549 cells, significantly enriched Gene Ontology (GO) terms and Reactome pathways were associated with mitochondrial translation, protein import, oxidative phosphorylation, and unfolded protein response (UPR), highlighting alterations in mitochondrial function and stress signaling. In contrast, HepG2 cells displayed enrichment of pathways linked to PI3K–Akt–mTOR signaling, amino acid and lipid metabolism, and detoxification processes, consistent with the hepatic role in xenobiotic metabolism. Apoptosis- and cell cycle–related pathways were also detected across both cell types.

Together, these findings demonstrate that short-term, low-dose PFOA exposure elicits distinct transcriptomic perturbations in A549 and HepG2 cells, converging on mitochondrial and stress-response pathways in lung cells and on metabolic regulation in liver cells. This work provides a comparative perspective on PFOA-induced transcriptional changes and highlights potential cell type–specific vulnerabilities.