

Toxic Mechanisms of Per- and Polyfluoroalkyl Substances Within Yeast Cells: Environmental and Human Health Impact

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Per- and polyfluoroalkyl substances (PFAS) are a class of persistent environmental contaminants known to disrupt biological systems across multiple trophic levels, yet their cellular and molecular effects in fungi, as well as humans, remain poorly characterized. This study investigates how three common PFAS compounds—perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), and perfluorobutanoic acid (PFBA)—affect the growth and gene expression of *Saccharomyces cerevisiae*, a eukaryotic model organism widely used for toxicogenomic research due to its genomic similarity to humans. Growth assays revealed concentration-dependent reductions in yeast viability for all PFAS compounds tested, with PFOS producing the greatest inhibition, followed by PFOA and PFBA. To further understand the mechanism of PFOA-induced stress, RNA sequencing was conducted on treated yeast samples. Differential gene expression analysis revealed substantial transcriptional difference, characterized by downregulation of genes involved in mitochondrial energy metabolism, and upregulation of pathways associated with nucleotide synthesis and cell cycle regulation. Collectively, these changes suggest that PFOA exposure disrupts core metabolic networks and induces a stress response in yeast aimed at preserving cellular integrity under toxic conditions. This work addresses a major knowledge gap in PFAS toxicology by being among the first studies to characterize their genomic effects in yeast. The results provide new insight into how PFAS compounds impair yeast metabolism/gene regulation at a fundamental level, offering a foundation for future investigations into the toxicity mechanisms and treatments.

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