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Bisphenol A alters energy metabolism and promotes a cancer-like transcriptomic state in non-cancerous breast cell lines

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Bisphenol A (BPA), a chemical widely used in plastics, is a source of exposure for both humans and animals. While numerous studies have shown that BPA promotes cancer cell proliferation in various cancer cell lines, such as hormone-sensitive cancer cell lines and colon cancer cell lines, its effects on non-cancerous cell lines and their potential role in early cancer development remain poorly understood. This study investigates the cellular responses to BPA in multiple non-cancerous cell lines from different tissues, which may contribute to cancer-related transformation. We used bulk RNA sequencing datasets obtained from Gene Expression Omnibus (GEO) and The Library of Integrated Network-Based Cellular Signatures (LINCS) to analyze cell lines before and after perturbation with BPA. Gene set enrichment analysis revealed that multiple energy-related biological functions were affected in MCF-10A, MCF-12A, and IOSE-80. BPA exposure also significantly impacted hallmark cancer pathways in MCF-10A, MCF-12A, IOSE-80, and OF-1. Notably, BPA-treated breast epithelial cells (MCF-10A, MCF-12A) exhibited transcriptomic shifts toward the cancer-like profile of MCF7 in PCA. These findings suggest that BPA

exposure alters energy-related pathways and drives non-cancerous breast cell lines toward a cancer-like transcriptomic profile, indicating a potential role in the initial transcriptomic changes associated with tumorigenesis.