

BIS(2-ETHYLHEXYL)-2,3,4,5-TETRABROMOPHTHALATE ENHANCES *FOXO1*-MEDIATED LIPOPHAGY TO REMODEL LIPID METABOLISM IN ZEBRAFISH LIVER.
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An emerging environmental contaminant, bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH), can bioaccumulate in the liver and affect hepatic lipid metabolism. However, the in-depth mechanism has yet to be comprehensively explored. In this study, we utilized transgenic zebrafish Tg (*Apo14: GFP*) to image the interference of TBPH on zebrafish liver development and lipid metabolism at the early development stage. Using integrated lipidomic and transcriptomic analyses to profile the lipid remodeling effect, we uncovered the potential effects of TBPH on lipophagy-related signaling pathways in zebrafish larvae. Decreased lipid contents accompanied by enhanced lipophagy were confirmed by the measurements of Oil Red O staining and transmission electron microscopy in liver tissues. Particularly, the regulatory role of the *foxo1* factor was validated via its transcriptional inhibitor. Double immunofluorescence staining integrated with biochemical analysis indicated that the enhanced lipophagy and mitochondrial fatty acid oxidation induced by TBPH were reversed by the *foxo1* inhibitor. To summarize, our study reveals, for the first time, the essential role of *foxo1*-mediated lipophagy in TBPH-induced lipid metabolic disorders and hepatotoxicity, providing new insights for metabolic disease studies and ecological health risk assessment of TBPH.