Cyclophosphamide in *Drosophila* promotes genes and transposable elements differential expression and mitochondrial dysfunction

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Abstract

Cyclophosphamide (CPA) is an alkylating agent used for cancer chemotherapy, organ transplantation, and autoimmune disease treatment. Here, mRNA sequencing and high-resolution respirometry were performed to evaluate the alterations of *Drosophila melanogaster* gene expression fed with CPA under acute (0.1 mg/mL, for 24 h) and chronic (0.05 mg/mL, for 35 days) treatments. Differential expression analysis was performed using Cufflinks-Cuffdiff, DESeq2, and edgeR software. CPA affected genes are involved in several biological functions, including stress response and immune-related pathways, oxi-reduction and apoptotic processes, and cuticle and vitelline membrane formation. In particular, this is the first report of CPA-induced mitochondrial dysfunction caused by the downregulation of genes involved with mitochondria constituents. CPA treatment also changed the transcription pattern of transposable elements (TEs) from the *gypsy* and *copia* superfamilies. The results presented here provided evidence of CPA mitochondrial toxicity mechanisms and that CPA can modify TEs transcription in *Drosophila* flies.

Keywords

RNAseq; Chemotherapy; Mitochondrial dysfunction; Prophenoloxidase; Transposable elements; *Turandot*.