THE EFFECTS OF TAMOXIFEN ON THE TRANSCRIPTIONAL PROFILE OF OVARIES OF TUMOR-BEARING RATS TREATED WITH CYCLOPHOSPHAMIDE

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Abstract Body

Chemotherapy drugs including cyclophosphamide (CPA) have a profound impact on ovarian functions leading to the depletion of the follicle reserve and, in consequence, to infertility of cancer patients. Our recent reports indicated that tamoxifen (TAM) can alleviate the adverse effects of CPA on follicular reserve both in cancer-free and tumor-bearing rats. The aim of the current study was to examine the mechanism of chemoprotective effects of TAM on the ovaries of tumor-bearing rats. To meet this goal we examined the effects of TAM on the gene expression profile in tumor-bearing rats treated with CPA. The female Wistar rats were treated weekly with CPA (1^{st} week: 50 and2^{nd}-5^{th} weeks 10 mg/kg b.w) and/or TAM (implant; 1 mg/kg b.w./d; 31 days). At the end of the experiment the ovaries were collected (n=4), total cellular RNA was isolated and designated for RNA-Seq. Following sequencing, 597 differentially expressed genes (DEGs; $p_{adjusted} < 0.05$ and log2FC ≥ 1.0) were identified using DESeq2. The expression of 340 DEGs was up-regulated and 257 DEGs was down-regulated by TAM in the ovaries of rats receiving CPA. The log2FC value for DEGs ranged from -7.49 (*cysteine-rich secretory protein 3*) to 63.67 (ENSRNOG00000051838). The DEGs classified into Gene Ontology database were mainly annotated to “receptor regulator activity”, “positive regulation of cell adhesion” and “organic hydroxy compound metabolic process” terms. The results of the current study contribute to better understanding of the protective mechanisms of TAM in the ovaries of rats undergoing cancer chemotherapy. Identification of genes that are crucial for TAM action in the ovary may inspire future researchers to find new and efficient strategies for women fertility preservation during cancer treatment.

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