THE EFFECTS OF INDIVIDUAL ADMINISTRATION OF CYCLOPHOSPHAMIDE AND TAMOXIFEN ON THE GENE EXPRESSION PROFILE OF THE OVARIES IN TUMOR-BEARING RATS

Orlowska, Karina[1]; Ruszkowska, Monika[1]; Nynca, Anna[2]; Sadowska, Agnieszka[1]; Swigonska, Sylwia[2]; Molcan, Tomasz[1]; Myszczynski, Kamil[3]; Petroff, Brian K.[4]; Ciereszko, Renata E.[1,2]

[1]Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury, Olsztyn, Poland, [2]Laboratory of Molecular Diagnostics, Faculty of Biology and Biotechnology, University of Warmia and Mazury, Olsztyn, Poland, [3]Department of Botany and Nature Protection, Faculty of Biology and Biotechnology, University of Warmia and Mazury, Olsztyn, Poland, [4]Department of Pathobiology and Diagnostic Investigation, Michigan State University, East Lansing, Michigan, USA

Abstract Body

Cyclophosphamide (CPA), a widely used anticancer drug, acts by chemical interactions with DNA contributing to the apoptosis of cancer cells. In the ovary, CPA causes depletion of follicles. Very recently, tamoxifen (TAM), a selective estrogen receptor modulator was shown to decrease loss of ovarian follicles in cancer-free and tumor-bearing rats treated with CPA. The aim of the current study was to examine the individual effects of CPA and TAM on the ovarian transcriptome of tumor-bearing rats. By employing RNA sequencing (RNA-Seq) we aimed to identify genes potentially involved in the mechanism of CPA as well as TAM action in the ovaries of female rats. To meet this goal, tumor-bearing Wistar rats were randomly assigned to: 1/ control untreated group, 2/ TAM-treated group (implant; 1 mg/kg b.w./d; 31 days) and 3/ CPA-treated group (1^{st} week: 50 and 2^{nd}-5^{th} weeks 10 mg/kg b.w). The ovaries were collected at the end of the experiment (n=4). RNA was isolated from the ovaries and sequenced using NovaSeq6000 high throughput sequencing instrument (Illumina). A total of 529 differentially expressed genes (DEGs; $p_{adjusted} < 0.05$ and $log2FC \geq 1.0$) were identified after TAM treatment (210 up- and 319 down-regulated) in comparison to control tumor-bearing rats. Most of DEGs were ascribed to metabolic-related Gene Ontology (GO) terms. CPA, in turn, affected the expression of 85 (34 up- and 51 down-regulated) genes and most of them were ascribed to GO terms associated with immunological processes. This study offers broader insight into the mechanism of CPA and TAM action in ovaries and provides a foundation for future research focused on molecular effects exerted by these chemicals.

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