The impact of tamoxifen on active DNA demethylation in breast cancer cell lines

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The active DNA demethylation process, which involves TET and AID family proteins, can affect DNA methylation pattern. TET dependent demethylation contributes to DNA hypomethylation by oxidation 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC) and its derivatives, whereas AID is possibly implicated in deamination of 5–hmC to 5–hydroxymethyluracil (5–hmU). Moreover, epigenetic processes, including DNA methylation, may affect regulation of genes involved in drug responses and drug targets. Tamoxifen is a leading drug in breast cancer hormonal therapy, which belongs to selective estrogen receptor modulators (SERMs). It has the ability to act like estrogen or antiestrogen depending on the receptor type to which it is bond: G–protein coupled or estrogen nuclear receptor, respectively. Thus, tamoxifen's pharmacological activity may be more complex than just controlling the estrogen signaling. Therefore, we tried to verify if SERMs supplementation of breast cancer cells may evoke changes in DNA methylation pattern. The study involved three breast cancer cells lines with differently expressed hormone receptors, which were supplemented with estrogens and the active derivatives of tamoxifen. We applied qRT-PCR and Western Blot for analyses of gene expression and protein levels involved in active demethylation process, and 2-D HPLC with tandem mass spectrometry detection for 5–mC and its derivatives assessment. We found differences between dissimilarly treated cells. The expression levels of TET2 and TET3 were dependent on the doses of the drugs. Furthermore, the distinctness in 5-mC level was also observed. According to our study, epigenetic changes in DNA are closely linked to cancer treatment. Our initial research may pave the way for new diagnostic and therapeutic methods as well as innovations in personalized medicine approaches.

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