

ESTROGEN RECEPTOR β AGONISTS ATTENUATE MITOCHONDRIAL BIOGENESIS AND PROMOTE CELL GROWTH IN MCF-7 BREAST CANCER CELLS.

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Breast cancer is common disorder among women and estrogens are involved in two-third of breast tumors. Estrogens bind with estrogen receptor in cell, and translocate to nucleus as transcription factors to activate a series of growth factor expression and promote tumor growth. During tumor growth, tumor cell favors anaerobic glycolysis to generate ATP. Previous study demonstrated that cytoplasmic estrogen receptor β (ER β) indicates the poor prognosis. ER β could locate in mitochondria but its mechanism remained unclear. In this study, we hypothesize that ER β agonist could attenuate mitochondrial biogenesis, inhibit ATP production from TCA cycle, accumulate lactate, and promote tumor cell proliferation. This hypothesis matches with the Warburg effect. In this first, ER β was detected in mitochondria in the MCF-7 breast cancer cells. The effect of ER β agonists diarylpropionitrile (DPN) and 17 β -estradiol (E2) was addressed. In MTS assay and cell growth count, MCF-7 cell would proliferate on E2 or DPN treatment. Mitochondrial biogenesis (mRNAs and respiratory complex proteins), ROS generation, ATP synthesis, pyruvate dehydrogenase (PDH) level, and mitochondrial membrane potential were all decreased on E2 or DPN treatment. But an increase in hypoxia-inducible-factor 1 α (HIF-1 α), pyruvate dehydrogenase kinase (PDK), lactate dehydrogenase (LDH) activity, and glycolytic enzyme phosphofructokinase (PFK) were identified on E2 or DPN treatment. According to above results, we demonstrated that ER β agonists could reduce mitochondrial biogenesis and induce MCF-7 favor hypoxia condition to promote cancer to growth.

Key words:

breast cancer, estrogen receptor β , mitochondria, diarylpropionitrile, 17 β -estradiol