Estradiol and/or ERs inhibits human LoVo colorectal cancer cells metastasis is mediated through tumor suppressor p53

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Abstract

The protective role of 17β-estradiol in carcinogenesis has been examined extensively. Epidemiologic studies suggest that men are more susceptible than women to develop colorectal cancer at all ages. Furthermore, hormone replacement therapy (HRT) have been reported to reduce the risk of colorectal cancer for postmenopausal women. At the same time, over-expression of mutant tumor suppressor protein p53 is one of the most frequent genetic alterations in human cancer and plays a critical role in carcinogenesis, affecting tumor development, progression and resistance to therapy. Approximately 50% of human cancers have p53 loss of function. Hence, the aim of this study was to investigate the effects of 17β-estradiol via estrogen receptors or

directly administration of ERs agonist on the development of human colorectal cancer, and to elucidate whether the effect was regulated by tumor suppressor gene p53. Here, our results showed that 17β-estradiol and/or ERs agonist treatment in human LoVo colorectal cancer cells could active p53, then up-regulated p21 and p27 protein level, subsequently inhibited downstream target gene, cyclin D1, which regulated the cell proliferation. In addition, 17β-estradiol and/or ERs agonist significantly reduced the level of uPA, tPA, MMP9 and β-catenin, which regulate cell metastasis. Conclusion, our findings demonstrate, the anti-tumorigenesis effects of17β-estradiol and/or ERs agonist suggests a possibility of using ERs selective agonist may prove to be an attractive alternative therapy in the treatment of human colorectal cancer.

Keywords: Estrogen, Estrogen receptor, Human colon cancer cell, p53