Synopsis of Original Research Paper

Molecular mechanism of estrogen against the senescence of skin cells.

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Telomerase activity is present in most malignant cells and provides a mechanism for the unlimited potential for division on neoplastic cells. Although telomerase is known to be regulated by several factors, the roles of sex steroid hormones have not been understood in target tissues such as breast, uterine endometrium and skin. In the series of our studies, we have examined the effect of sex steroid hormones including estrogen, progesterone and SERM on the telomerase activity and investigated the molecular mechanism of their effects. Estrogen has up-regulated telomerase activity as well as hTERTmRNA in ER-positive cells. Gel shift and luciferase assays have revealed that estrogen-responsive element of hTERT promoter sequences is responsible for transcriptional activation by activated ER. Estrogen has also activated c-Myc expression and then it has been cleared that c-Myc/Max play additional role in estrogen-induced transactivation of hTERT. On the other hand, progesterone significantly induced hTERT mRNA expression in short-time exposure and inhibited the estrogen-induced activation of hTERT expression in long time exposure. The p21/Waf1/Cip1 played an integral role in this inhibition. SERM has up-regulated hTERTmRNA in uterine endometrial cells and down-regulated in breast cancer cells. hTERT protein was immunohistochemically detected in stem cells of the skin. The immortalized cells with normal structureal and functional characteristics which we have established could be a powerful tool for the understanding of the roles of sex steroid in aging and the clinical application.