

P338. Does Norethisterone stimulate human breast cancer cells proliferation by promoting PGRMC1 expression?

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Context :

Important studies such as the Women's Health Initiative (WHI) and the Million Women Study (MWS) showed progestogens may play a important role in the development of breast cancer under hormone therapy in menopausal women. Progesterone receptor membrane component 1 (PGRMC1) has been found to be highly expressed in the tissue of breast cancer patients.in our previous studys,we found norethisterone (NET) can stimulate the proliferation of breast cancer cells which express PGRMC1 in vitro and in vivo,However the mechanism is unclear.

Objective:

To investigate possible mechanisms for increased breast cancer risk with NET in hormone therapy and oral contraceptives.

Methods: Cell viability assay was performed to investigate the proliferation effect of MCF-7 cells stimulated with NET or progesterone (10-5 M~10-11 M).Quantitative PCR and Western blot analysis were used to evaluate the PGRMC1 expression in three groups. The promoter sequence of PGRMC1(2kb) was cloned into pGL3-basic reporter vector. Cells were transfected with plasmids using FuGene. Luciferase activity was determined 48 hours posttransfection with the Dual-Luciferase Reporter Assay System .

Results:

NET induced MCF-7 cell viability dose-dependently, but this effect was not observed by using progesterone. Our real-time quantitative PCR data displayed the significantly increase mRNA level of PGRMC1 in the MCF-7 cells stimulated with NET dose-dependently. Western blot analysis show that expression of PGRMC1 in protein level significantly increase in the MCF-7 cells stimulated with NET compare to MCF-7 cells stimulated with progesterone.We found NET up-regulated the activity of the PGRMC1 promoter.

Conclusion:

NET increases the proliferation of breast cancer cells maybe by PGRMC1. We have demonstrated for the first time that NET can up-regulated the activity of the PGRMC1 promoter to increase expression of PGRMC1.

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