Abstract

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Retinoic acid modulates prolactin receptor expression and prolactin-induced STAT-5 activation in breast cancer cells in vitro.

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BACKGROUND: Two recent papers demonstrate that prolactin plays an important role in the induction and progression of mammary tumours. Retinoids have been shown to be potent inhibitors of breast carcinogenesis.

OBJECTIVE AND METHODS: We studied expression of prolactin receptor mRNA in human breast cancer cell lines MCF-7, SKBR-3, T47D and BT-20 treated with and without retinoids using Northern blot and a quantitative polymerase chain reaction (PCR) method.

RESULTS: In all cell lines, all-trans- and 9-cis-retinoic acid, as well as the retinoic acid receptor gamma (RAR-gamma) selective agonists CD2325 and CD437 (1 microM), were able to down-regulate prolactin receptor. After 1 h, a significant reduction was detectable and maximal effect was achieved after 24 h of treatment. Pretreatment with retinoic acid also reduced the prolactin-/prolactin receptor-dependent signal transduction and activation of transcription 5 (STAT-5) activation in T47D cells. Cycloheximide failed to abrogate the retinoic acid-induced decline in prolactin receptor mRNA levels, indicating that this effect was not dependent upon continuing protein synthesis. Similarly, no change in the stability of prolactin receptor mRNA was observed during 12 h of retinoic acid treatment.

CONCLUSION: In conclusion, our results demonstrate that retinoids are able to inhibit the expression of prolactin receptor message, which encodes an important growth factor receptor in breast cancer cells. This action could be responsible for the anti-tumour effects of retinoids.

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