

Abstract

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S179D prolactin sensitizes human prostate cancer cells such that physiological concentrations of 1, 25 dihydroxy vitamin D3 result in growth inhibition and cell death.

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BACKGROUND: S179D Prolactin (PRL) is a molecular mimic of naturally phosphorylated human PRL which has been shown to inhibit the growth of human prostate cancer cells both in vitro and when grown as tumors in nude mice.

METHODS: In the current study, we have investigated the potential interplay between S179D PRL and 1,25 dihydroxy vitamin D3 (1,25D) in the inhibition of prostate cancer cell growth by incubating cells under circumstances where each hormone alone has no effect.

RESULTS: Incubation of DU145 or PC3 cells in 100 pM 1,25D or 10 nM S179D PRL for 3 days showed no effect of each alone on expression of the vitamin D receptor (VDR), or the cell cycle regulatory protein p21, or on cell number. Incubation in both together increased expression of the VDR and p21 two to threefold. This co-operative effect was reproduced when activation of the p21 promoter was analyzed using a p21-luciferase (p21-luc) construct. Elimination of the VDR response element from p21-luc eliminated response to the hormone combination, showing that the effect on p21 was through the VDR. Most importantly, S179D PRL sensitized the cells to 1,25D such that there was a concentration-related reduction in cell number versus controls between 40 and 160 pM. At least part of this effect was via the induction of cell death.

CONCLUSIONS: These results suggest that combined anti-tumor therapy may be very efficacious and that the dose of 1,25D required may be below the range that results in hypercalcemia.

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