Vitamina D3 e análogos aumentam a principal proteína anti-câncer humana, a p53

Vitamin D analogues increase p53, p21, and apoptosis in a xenograft model of human retinoblastoma.


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PURPOSE. To study the antineoplastic effect of vitamin D analogues in a xenograft model of human retinoblastoma. METHODS. Athymic mice were injected subcutaneously with Y79 cells and treated 5 days a week with either mineral oil (control group) or the vitamin D analogues calcitriol or 1,25-dihydroxy-16-ene-23-yne vitamin D(3) (16,23-D(3)). BrdU was injected 1 hour before death. Animals were killed after 1, 2, 3, or 5 weeks. Paraffin-embedded sections of the tumors were studied for cell proliferation by monitoring for BrdU incorporation and cell death by terminal transferase dUTP-nick end labeling (TUNEL), 3'-overhang ligation, and histology. Sections of the tumors were immunostained for p53 and p21. RESULTS. There was no significant difference in incorporation of BrdU among the three groups, suggesting that cell proliferation is unaffected by vitamin D analogues. TUNEL was increased in tumors treated with vitamin D analogues compared with the control group. This increase was statistically significant for calcitriol in the time frame examined, but not statistically significant for 16,23-D(3). Alternatively, the ratio of proliferation to cell death was significantly different for both calcitriol and 16,23-D(3) compared with control tumors after 3 weeks of treatment. Dying cells contained DNA strand breaks with overhanging nucleotides and nuclear changes characteristic of apoptosis. CONCLUSIONS. Vitamin D analogues appear to attenuate retinoblastoma tumor growth in athymic mice by increasing apoptosis. Cell death is associated with the upregulation of both p53 and p21. PMID: 14507860