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Pretreatment of prostate cancer cells with the active metabolite of vitamin D and sodium valporate enhances the effect of ionizing radiation

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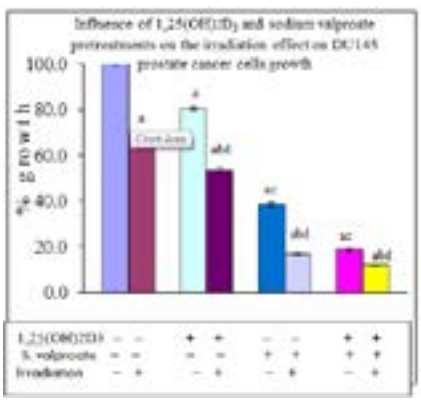
Ionizing Radiotherapy (IR) is known to be a general effective treatment of cancer including prostate cancer. However, this treatment causes many severe side effects. On the other hand, recent studies demonstrate the anti-carcinogenic activity of the active metabolite of vitamin D, namely 1, 25 dihydroxyvitamin D3 (1, 25(OH) 2D3). The aim of this study was to try to develop cancer–sensitizing pretreatments, based on 1, 25(OH)2D3, that may potentiate the therapeutic effect of IR. Such achievement will allow the use of lower radiation doses and limit its side effects. Toward this aim, we have incubated *in vitro* prostate cancer cells treated with 1, 25(OH)2D3 alone, or with combination with the anti-carcinogenic drug sodium valporate (VPA) before IR. The results show that while IR alone (4Gy) of DU145 line of prostate cancer cells decreased cell proliferation by 30.6%, IR after pretreatment with 100nM 1, 25(OH)2D3 and 1 mM VPA, efficiently suppressed cell proliferation by 87.9% ($p<0.0001$). On same time the combined pretreatment increased the DNA double-strand breaks by 58.1%, as compared to 11.8% in radiated cells without the pretreatment ($p<0.002$). The combined pretreatment enhanced IR induced cell cycle s-phase arrest and cell apoptotic death. These results confirm our hypothesis that pretreatment of prostate cancer cells with 1, 25(OH) 2D3, and specifically in combination with VPA, is highly efficient in potentiating the anti-carcinogenic activity of IR. Using such pretreatments would increase the therapeutic effect of IR and may allow the use of lower doses of IR with less severe side effects.



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Biography

Professor (Emeritus) Shraga Shany is a faculty member at the department of Clinical Biochemistry and Pharmacology at the Faculty of Health Sciences in Ben Gurion University of the Negev, Beer Sheva, Israel. He was graduated at the Hebrew University of Jerusalem. His main research interest is in the field of vitamin D. His studies and publications include the topics of vitamin D status and metabolism in uremia, in rickets, in fracture healing and in the elderly. Shany's research includes uncovering the effects of vitamin D on the immune system, emphasizing the auto-paracrine mode of action of 1,25-dihydroxyvitamin D in Inflammatory cells. Recently, professor Shany's studies are concentrated on the anti-carcinogenic activities of the active metabolite vitamin D, and of its analogs, alone, and in combination with other drugs and Radiotherapy. Professor shany has more than 140 peer reviewed publications with more than 3000 citations. Professor Shany is teaching clinical and basic biochemistry in the school of medicine, Faculty of Health Sciences, at Ben Gurion University.

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