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Role of vitamin D in modulation of MUC-1 in pancreatic cancer

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Over the years, pancreatic cancer has been established as a complicated disease with poor prognosis and survival rate. Standard chemotherapeutic agents/drugs have not shown any significant advancement in its regression. Several studies have indicated anti-angiogenesis and blocking the cancerous growth of breast, prostate, lung and colon by micronutrients like vitamin D, E and B12. Although, pancreatic cancer tissue expresses Vitamin D (VitD) receptor, the potential mechanism to exert anti-cancer effect remains underexplored. Thus, our study aimed to find out the mechanistic effect caused by the VitD analogue (calcitriol) in pancreatic cancer cells. Pancreatic cancer cells (PCC lines; MiaPaCa2 and PanC-1) treated with calcitriol for longer duration (24 hours to 96 hours) showed decreased expression of metastatic phenotype, CXCR4/CCL12, EpCAM/Vimentin along with decreased chemoresistant MUC-1 expression, although no inhibitory effect was observed on their proliferative capacity. But, addition of Gemcitabine (Gem) to calcitriol-treated PCC lines increased their apoptotic capacity than cells treated only with Gem, suggesting that calcitriol treated-PCC cells are susceptible to chemotherapeutic drug. Further, with the emergence of stroma playing a major role in pancreatic cancer, we attempted to elicit the involvement of VitD in Sonic HedgeHog (SHH) signaling. Enhanced apoptosis was observed when salinomycin (SHH inhibitor) was administered to calcitriol treated-PCC cells. Copy numbers of transcription factors C-myc, SMO, PTCH1, PTCH2 and hypoxia-induced factor (HIF1- α) were observed to show increased expression in treated PCC lines in comparison to untreated cells. In conclusion, our experimental evidence postulates a potential mechanism by which VitD-analogue; calcitriol modulated its stromal interaction via its action on the cell-membrane protein MUC-1.

Biography

Sangeeta Choudhury is an Associate Professor and Senior Consultant at Sir Ganga Ram Hospital, New Delhi, India. She has obtained her Doctoral degree from Bhabha Atomic Energy Research Centre, Mumbai, India. She was a Research Fellow at Department of Anatomy, Division of Cell Biology, University of New South Wales (UNSW), Australia and also completed her Postdoctoral Fellowship at Division of Infectious Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, USA. She has then joined as Research Scientist at Indian Council of Medical Research, National Institute of Immunology, New Delhi, India. She has been the recipient of national awards (Lady Tata Grants, Department of Atomic Energy, INDO-US Vaccine Action Program). Her major areas of interests are solid tumor biology and stem cell, cancer and obesity related metabolic disorders, transplantation immunology. She is in the Review Board of national journals and also scientific committee. She has authored about 28 scientific articles and three book chapters.

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