Down-regulation of $K_{Ca}3.1$ contribute to the antiproliferative effect of vitamin D receptor agonists in mouse preosteoblasts

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Vitamin D (VD) plays important roles in bone development indirectly via control calcium absorption in the intestine and reabsorption in the kidney. However, several in vitro studies showed that VD can directly suppress the cell proliferation of mouse osteoblasts. The intermediate-conductance Ca^{2+}-activated K^+ channel $K_{Ca}3.1$ regulates intracellular Ca^{2+} signaling pathways and is associated with cell proliferation in various types of cells. In the present study, treatment with VDR agonists for 48 h markedly decreased the expression levels of $K_{Ca}3.1$ transcripts and proteins in mouse preosteoblast MC3T3-E1 cells, resulting in the significant inhibition of Ca^{2+} rises induced by DCEBIO, a specific $K_{Ca}3.1$ activator. Treatments with VDR agonists also significantly decreased the expression of transcriptional regulators of $K_{Ca}3.1$ such as histone deacetylase 2 (HDAC2) and Fra-1 composed of activation protein 1. In addition, the siRNA-mediated blockade of VDR significantly rescued the decreased expression of $K_{Ca}3.1$, HDAC2, and Fra-1 protein in MC3T3-E1 cells treated with VDR agonists. Our results suggest that $K_{Ca}3.1$ is a new downstream target of VDR signaling and the down-regulation of $K_{Ca}3.1$ contributes, at least partly, to the antiproliferative effect of VDR agonists in mouse pre-osteoblasts.