Vitamin D_3 decreases glycolysis and invasiveness, and increases cellular stiffness in breast cancer cells

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Breast cancer is one of the major causes of death in the USA. Cancer cells, including breast, have high glycolysis rates to meet their energy demands for survival and growth. Vitamin D_3 (VD_3) is important for many important physiological processes such as bone mineralization, but its anticancer role is yet to be proven. We find that VD_3 treatment significantly downregulates glycolytic enzymes, genes, and decreases glucose uptake - for both lowly metastatic MCF-7 and highly metastatic MDA-MB231 (MB231) breast cancer cells. VD_3 also significantly decreases cell viability by inducing apoptosis - consistent with decreased expression of mammalian target of rapamycin (mTOR), which regulates glycolysis and cancer cell survival, and increases 5' adenosine monophosphate-activated protein kinase (AMPK) activation. These changes accompany a significant reduction of cell migration and increased cell stiffness - presumably a consequence of reversal of the epithelial to mesenchymal transition resulting in increased E-cadherin and F-actin expression. High levels of cytoskeletal and cortical F-actin may cause high cell stiffness. VD_3 induced mechanical changes are stronger in highly metastatic MB231 than in lowly metastatic MCF-7 cells. Our results suggest therapeutic and preventive roles of VD_3 in breast cancer.

Keywords: Breast cancer, Vitamin D_3, glycolytic enzymes, cell mechanics, cell migration, EMT.